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EMIL KRAEPELIN, THE MAN AND HIS WORK*

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Memorials to the lives and deeds of men are carved in stone and cast in bronze. These are permanent reminders of those who have rendered service valued by their fellow men. There is a different sort of monument with an endurance of another kind. Its greatness does not lie in its finished perfection as an imposing testimonial merely of what has been accomplished, but it has a functional greatness in that while it commemorates it also vitally links past achievement with future opportunity. Not only does it stand as a fixed record, but it likewise submits to changing needs and permits of adaptation to altering demands. Such are the memorials that perpetuate the life and work of Emil Kraepelin.

At once there comes to mind the most conspicuous of these, in its essential character representing consecration and continuous adaptation to the evolution of psychiatric knowledge and practice: the German Institute for Psychiatric Research at Munich, conceived and planned by Kraepelin's creative genius and brought to reality by his indomitable perseverance. This is, however, but one of the living testimonials by which the present scientific world and the future may remember and participate in the service to which Kraepelin's life was devoted. There are his writings, which embody his specific contributions to the progress of psychiatric theory; the ideals of his practice, his teaching and his indefatigable investigation; his social interests, extending beyond the strict borders of his own specialty; the hopes and plans for the type of research, in part fulfilled on his visits to the American continent and in part awaiting the travels of his pupils; then the more personal revelations of moods and longings contained in a posthumously published volume of poems, and a home established in Italy for retirement and quiet work and still preserved for his family and for members of his profession who may seek its shelter. These are all eloquent of the man whose life they express and of his provision that others may carry forward and share in the work he began.

A brief survey of the main facts of Kraepelin's life will lead to a fuller consideration of the monuments he has left. Kraepelin was

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strongly averse to biographic exploitation of personal matters as well as to personal adulation of any sort. He prepared for his immediate circle of friends and colleagues at their request an autobiographical sketch, but the facts of his life are but scantily recorded. He was born in Mecklenburg, Germany, in 1856. His medical education was obtained in Würzburg, Munich and Leipzig. His first contact with psychiatry at Würzburg came through the study of psychology with Wundt, and his interest in psychology led him to his choice of profession. When he took his degree under Gudden in Munich, the subject of his thesis was the "Place of Psychology in Psychiatry." He hoped much from the aid of psychiatry in the knowledge of normal psychology, but found that the time was not yet ripe, research had by no means proceeded far enough for the scientific application of psychology—the experimental psychology he had pursued—to psychiatric investigation. He was compelled in the pressure of investigation along other lines to leave more complete association of psychology and psychiatry to the future, although he continued in the development of certain functional curves which he plotted and on which he laid great stress. It may be remarked in passing that this interest in psychology kept itself aloof from subjective psychology almost to the end of his life. Kraepelin had a great distrust of the admission of the subjective and emotional into research, believing that here the foundations were not yet sufficiently laid in actual scientific knowledge and that such an approach could prove only a snare to the student of fact. The "natural sciences" were the true basis of psychiatric study and their aid must be solicited to the fullest capacity to contribute to psychiatric knowledge.

Kraepelin's personal nature was guarded by a wall of reserve. He held himself sternly to his goals; he devoted himself unremittingly to his work, uncompromisingly following what he believed to be the path of investigation—exact, demonstrable and well established by the assembling of all possible testimony step by step. It was consistent with this nature and its attitude that only the precision of experimental psychology should seem applicable, that the more elastic boundaries of a subjective psychology of mental disease, like psychoanalysis, should seem forbidden and untrustworthy territory. In the summer before he died, however, when I saw him at Suna, he was much more prepared to discuss sympathetically the freudian psychiatry than even two years previously, when I also had visited him on Lago Maggiore.

Early in his career Kraepelin had made deliberate choice of the field of psychiatry, looking forward to the service of teaching and investigation. After taking his degree under Gudden in Munich, he became assistant of Flechsig in Leipzig. His work as professor of psychiatry began first at Dorpat. Here, working along side of Kobert, he early became interested in drug actions. He continued his professional career

at Heidelberg, where he revealed his genius for organization and development of his subject in association with Aschaffenburg, Nissl, Alzheimer, Gaupp and others. In 1906 he was called to Munich, where he took charge of the new clinics still building, and where through the years that followed he pursued his plans in regard to the establishment of the now existing Psychiatric Institute.

I first worked at the new Munich clinic in the summer semester of 1906. Dr. Pearce Bailey and I traveled together, and I spent six months in the clinic with Kraepelin and in the laboratory with Alzheimer. Scripture was also attending the clinical lectures, and Cotton was busy in Alzheimer's laboratory. There was an enthusiastic group of assis-

Summer semester group, Munich, 1906. From left to right, sitting: Hermann, Wüttenberg, Gaupp, Scripture, Cotton, Flatau, Achucarro, Allers (?), Gudden; standing: Alzheimer, Röhde (?), Kraepelin, Dreyfuss, Jelliffe, Perusini, Bailey, Busch, Probst, Rehm, Lüttge.

tants and workers in the clinic. Parhon from Roumania was there, Sibelius from Helsingfors, Lundborg from Sweden and others.

It was Kraepelin's yearly custom to take walks with as many of the assistants and workers as cared to. They were facetiously known as the "Katatonic Walks," but it was on one of these, a reproduction of the participants of which is here given, that I was fortunate in getting a little closer to Kraepelin than through the more formal periods of round making, lecture attendance or laboratory work. He learned on this walk that I was interested in botany, and as he was an enthusiastic botanist himself, I had a most delightful contact through this channel as well, a contact that persisted through the twenty years of

our friendship. In response to my inquiries about the flora of Bavaria, for it was in full progress of blooming, we traveled into the fields for specimens which were all unknown to me, save as to their family alliances. I was quite ignorant of the species of many of the flowering plants, which he told me. I was able to keep my end up in the cryptogams with which Kraepelin was not so well acquainted. Thus through a mutual interest outside of psychiatry was opened up a side of Kraepelin's nature which drew him to me in a special way. We were always friendly and in accord in this field, even though he felt somewhat doubtful when in later years, 1914 and 1921, the latter particularly, my interest in psychoanalysis offered many hours of earnest discussion.

Kraepelin's supremely controlling object was the furtherance of psychiatry through the actual work of its daily practice and the extending of its knowledge by the assemblage of the multitude of facts which daily work and observation would bring. His mind was capable of large conceptions by which he outlined his field before him. But he was no visionary; he knew and pursued but one way of achieving results, through detailed development and application of method and collection of observed data. His own hand was constantly at work on his accumulating material that nothing might escape him. It was thus that he combined and tested in ever new experimental classifications. Intuition provided its inspiration, but he was too rigidly disciplined—a trifle too rigid perhaps—to permit speculation too free a hand. Out of such work grew his system of psychiatry as given to the world in his personal teaching and in his writings, chiefly his well known "Text Book of Psychiatry," the ninth edition of which was in preparation when he died and of which he had completed volume 2 on "Special Psychiatry."

Kraepelin can with reason be called the greatest systematizer of psychiatry of the present era. There have been such systematizers before him, from Asclepiades of Bithynia onward. There have been great periods of active analysis, which have then been gathered into a masterly synthesis. Following the "manic" period of analysis of Linnaeus there was the ultrarigid reduction of Pinel, which almost regressed to the oversimplification of the work of Felix Platter. So from the days of the older Falret, through Hecker and Kahlbaum a new period of analysis took place. Kraepelin achieved a new important synthesis of this period. By following disorders from their first symptoms in the earliest stages to the complete working through, he arrived at a natural history grouping. In this basis prognosis and therapy could be determined and prophylactic work undertaken to advantage. Two disease groups, if similarly located, must manifest identical psychic disturbances, he argued, while special areas are specially disposed to disease. His vast material of clinic and laboratory, arranged and rearranged by his untiring hand, supported his conceptions even while it led to modifications of them. The early concept of secondary dementia of his

teachers was rejected, while his attention was directed more specifically to the diagnostic discovery of the causes, the course and the outcome of the mental disorders with reference to specific lesions involved. Very early he sought to understand the relation of psychoses to infectious diseases. He kept before his mental eye a perspective of trends, one might say, which would culminate in various types and degrees of deterioration. Time has already brought alterations in the conceptions Kraepelin advanced, and his groupings are being subjected again to the analytic process; nevertheless, the foundation he laid for a unified and comprehending psychiatry and the direction he gave toward progressive research will always represent a highly significant stage in the history of psychiatry.[1]

Kraepelin impressed on his work as a teacher the qualities of character which marked his research, his effort being directed always to the goals that were his for psychiatry as a whole. His students were in large part neuropsychiatrists from all parts of the civilized world. He was as stern and unyielding with others as with himself. He never compelled his students and fellow workers to his way of thinking or to accept his convictions, yet his own vast extent of knowledge, his powerful self-control toward his goals and his untiring energy created a power behind his guidance of those who worked with him. His own mind was too fertile, his sympathies too generous despite his reserve and his conception too broad to admit of a servile adherence on the part of his disciples. Such an attitude would have been repugnant to him. He wanted workers about him who were free in mind, like himself, and open to the convincing instruction of observable facts.

As a physician in care of the mentally diseased his attitude was one of kindness illuminated by attention to every phase of the patient's well-being. His system of care was not governed by a spirit of restraint, but, on the contrary, it provided for the fullest permissible freedom for the personality submerged in its disorders. His wards were noted for the orderliness and quiet that prevailed. Great care was exercised

1. Meyer, Adolf: Kraepelin, Wernicke and Zielen: A Critique, in Church, A., and Peterson, F.: Textbook of Nervous and Mental Diseases, Philadelphia, W. B. Saunders Company. Jelliffe, S. E.: Some Historical Phases of the Manic-Depressive Synthesis, J. Nerv. & Ment. Dis. **73**:353, 1931; A Summary of the Origins, Transformations, and Present Day Trends of the Paranoia Concept, Med. Rec. **83**:599 (April 5) 1913; The Psychiaters and Psychiatry of the Augustan Era, Bull. Johns Hopkins Hosp. **19**:308, 1908; Manic Depressive Psychosis, Kansas City M. Index-Lancet **31**:111, 1908; Dementia Praecox: An Historical Summary, New York M. J. **91**:521 (Feb. 19) 1910; Cyclothymia: The Mild Forms of Manic-Depressive Psychosis and the Manic-Depressive Constitution, Am. J. Insan. **67**:661, 1911; Psychiatry of Our Colonial Forefathers, Arch. Neurol. & Psychiat. **24**:667 (Oct.) 1930.

in the selection of staff assistants, nurses and attendants, and there was also intelligent separation of disorders one from another.

Kraepelin's social interests extended themselves actively outside the more strictly limited field of his own specialty. His strong sense of right was roused wherever injury threatened or injustice was done. He did not shrink from expenditure of time and effort to right a wrong. Such an instance, for example, is related of him in his espousal of the cause of a patient brought to him from the penitentiary as a querulant, but whom Kraepelin recognized as one with a just cause of complaint. The man was serving a sentence for homicide, but his innocence was proved and finally admitted only through Kraepelin's unremitting efforts, despite most difficult obstacles in the way. Kraepelin as a young man anticipated the movements of a later criminology in advocating a treatment of criminals, having its basis not in the retaliation and revenge of society on the culprit, but in the principle of the welfare of society. Thus the injury should be made good as far as possible and the offender should be brought as far as could be to reform or should be rendered harmless. The death penalty and corporal punishment Kraepelin condemned as extremely barbarous and brutal. He urged parole with surveillance instead of ordinary punishment, at the same time laying the greatest emphasis on education. Work should be considered an indispensable aid, but while it should be required, it should never be forced labor. Such a program would rightly necessitate a large and varied staff of trained workers, for all of which he patiently awaited future development. Kraepelin was keenly interested in the problem of alcholism, both in its social aspect and as a matter of psychiatric investigation. He devoted much specific study to the latter phase.

Chock full of humor as he was, witty and alert to see a joke and as equally quick with a comeback, concerning alcoholism Kraepelin never could get away from its serious aspects. His own highly sublimated antisocial tendencies rarely could countenance even the slightest "cracks" about alcoholism. It was a great blow to him to note the American prohibition situation as it actually existed on the occasion of his last visit to the United States (1923-1924). The great white way of Broadway was an amazing sight to him. I think next to his keen delight in fresh pineapple, Broadway pleased him. We gave him pineapple and Broadway every day for the two or three weeks he and Plaut were our guests.

We also gave him a front room in the house where directly in front of his window he could observe at his leisure, and all day or night as he chose, the actual workings of the prohibition question—observable through two "speakeasies" across the street. He was amazed to note the number of policemen who went in and out almost wiping the beer foam from their lips. It was a constant marvel to him as we showed him

place after place where this "Noble Experiment" was being evaded. He never grasped the hypocrisy of it all, least of all how the citizens could stand it. Jokes about "prohibition" always seemed to wound him, and "it" and the "war" were taboo at our family table with or without guests.

Epilepsy and thyroidism, together with the whole subject of metabolic activity, the chemistry of disease, were objects of Kraepelin's active inquiry. He entered into the problem of the effect of drugs, medicinal or habitual, and the nature of sleep, attention, fatigue and the like.

It was given Kraepelin to combine these interests finally in one great center of research where the relation of all these branches of science to mental disease may be examined and these various territories explored for their contribution to psychiatric knowledge and practice. But it was not until after years of planning, labor, discouragement and hope deferred that this realization became possible, and then—so strange is fate—Kraepelin could only leave the fulfilment of his dream in the hands of his successors to carry on the research he had planned. Plaut tells us of his remark as they stood together before the statue of Moses in the Library of Congress at Washington two years before Kraepelin's death: "I shall meet the same fate as Moses. I shall see the Promised Land from afar and then lay myself down and die." Like Moses he came to the very borders of the Promised Land toward which he had led his followers, to which he had journeyed by a protracted route through the wilderness of postwar difficulties, and there, almost at the opening of the institute, he closed his eyes in death.

As has been noted, when Kraepelin went to Munich in 1904 after his eight years' professorship in Heidelberg, he went to a clinic and a psychologic laboratory only partially developed. The building at 7 Nussbaumstrasse was there, but the personnel was to be fitted to it. He applied his abilities as organizer to the task in hand and absorbed himself in the plan which he nurtured through the succeeding years, the building of a research institute where each science could be independently pursued but in harmonious service to psychiatry. He outlined his scheme before a conference in Breslau in 1916. In the spring of 1918 the institute was opened in the rooms of the Psychiatric Clinic of Munich with the expectation that with the end of the war it would pursue its work in halls of its own. Then came, however, the period of inflation followed by the further financial distress at the return to standard currency, when the continuation of the existence of the institute stood in imminent danger. It was rescued in the first instance by Dr. James Loeb, who with Dr. Krupp von Bohler and Halbach had been the largest contributors at the beginning; then at the second period

it was preserved from collapse by the aid of the Kaiser Wilhelm Gesellschaft. In 1924 it was made a member of the group of the Kaiser Wilhelm institutes, which guaranteed its further existence since it was the recipient now of funds from the Kaiser Wilhelm Gesellschaft and from the government.

Nevertheless, these provisions were only for the carrying on of its work, which still needed a home of its own for its proper development. For the present it had to be content with the space granted it in the Psychiatric Clinic and other scattered quarters, wherever they could be rented. It was then that Kraepelin succeeded in obtaining from the Rockefeller Foundation the sum of $250,000 for his project, the first gift to be made by this organization to research work in Europe. A further gift from the Rockefeller Foundation increased this sum to $325,000 under the stipulation that there should be strict adherence in the institute to Kraepelin's fundamental idea and his plans, an agreement that was assumed by Kraepelin's colleagues, for the latter gift was awarded only after Kraepelin's death, in answer to a final plea in his last letter. Then 300,000 marks, or about $60,000, were added to the sum: through a gift from Alfred Heinsheimer, contributions from the Kaiser Wilhelm Gesellschaft and the city of Munich and from funds from the institute's own work. Munich gave the right to the land on which the building was to be erected adjoining the Schwabinger Hospital.

In January, 1927—Kraepelin had passed away in the previous year at the age of 70—the work on the new building was begun, and by the end of March, 1928, it was possible for the work to be opened up at last within the walls. The official dedication took place during the meeting of the Kaiser Wilhelm Gesellschaft in Munich, on June 13, 1928. Representatives of psychiatry and neurology from various countries participated in the ceremonies in commemoration of the leader whom the institute proclaimed, but who himself had had to relinquish his task to other hands. On the occasion of Kraepelin's seventieth birthday, an international committee had been appointed, its members being drawn from among his colleagues in many lands, to collect a sum of money which might be contributed toward the preservation of the institute. It was but a modest sum, and it was rendered unnecessary for its original purpose by the gift of the Rockefeller Foundation. When, therefore, it was presented to Kraepelin on his birthday he requested that the income from it should be used to assist talented young research workers. Besides this prize, the committee decided to award from the same source a Kraepelin medal to be given on special occasions for distinguished service in research. At the dedication of the institute, therefore, the first of these medals was presented to

Dr. Oscar Vogt, who together with his wife, Dr. Cecilia Vogt, had done much of his work on the cerebral cortex to support the conceptions and findings of Kraepelin in regard to the physical basis of mental disease. The medal bears the Greek inscription: "Λαμπάδας ἔχοντες μέρα διδόντων ἀλλήλοις" ("Those who bear the light pass it on to others"). This may well be the fitting watchword that sums up Kraepelin's ideals for his institute.

The arrangement of the institute in its architectural structure is designed for the fulfilment of these ideals. The realization of Kraepelin's wish that all departments should be conducted in perfect equality of rank and in mutual service to the fundamental aims of the institute is provided for in the division into rooms devoted to the various departments of science: psychology, anatomy, histopathology, serology and experimental therapy, chemistry, the study of spirochetes, heredity, and so on. There are also a department for the *Klinisches Archiv* and for genealogy, a library and an auditorium. A connecting passage leads to the psychiatric division of the Schwabinger Hospital, which was built by the city of Munich in response to Kraepelin's request. Thus practical contact with actual psychiatric material is added to the laboratory work of the institute itself. A bust of Kraepelin stands in the entrance hall, where there also is a tablet with an inscription in German, which may be rendered as follows:

German Institute for Psychiatric Research
the work of Emil Kraepelin
Established by means of generous endowments
in the year 1914
Joined to the Kaiser Wilhelm Society for the
Promotion of the Sciences in the
year 1924
Presented with this Building by the Rockefeller
Foundation in the year 1928

Each department of the institute is the territory of a specialist, where he may work in perfect freedom of investigation; nor are these departments rigidly established in number and division. Changing needs in the course of time will demand alteration of plans as emphasis shifts from one branch of science to another, or new fields present themselves for admission and old ones prove no longer fertile. For this, ample provision is made in the flexibility of the institute in accordance with Kraepelin's desire. The management of the institute passes in turn from one to another of the investigators in the various departments; thus the absence of distinction in grades of authority is preserved, while the necessary centralization of administration is not lacking. The work, therefore, which Kraepelin planned and for which he made preparation

is being carried on by such men working in their fields of research as Spielmeyer, Plaut, Rudin, Jahnel and Spatz.

Kraepelin with Plaut visited America in 1924, when he extended his journey beyond the United States to Mexico and Cuba to study dementia paralytica in the Indian and the Negro. A similar journey to India with the same purpose in view was planned by Kraepelin, for which, indeed, his passage was engaged, when illness and death overtook him. Travel was always a joy to him, a means of recreation after arduous labor, and of delight in nature, which increased with the extent of his visits to all parts of the world and which found particular satisfaction in the luxuriance of the tropics. As he confesses in his autobiography, he gratified in travel that which was to him the deepest source of his inclination thereto, namely, an unrestrainable impulse toward freedom.

For Kraepelin, the man of iron will, disciplining and directing all his powers toward his life tasks, possessed also this strong urgency for freedom from constraint. He not only rejoiced in nature's display, in her moods, but he had a love of music, of fine literature, both of the latter being sacrificed, however, in large degree to the pressing demands of professional duty.

Kraepelin was not a man of intimate friendships. He was self-contained, absorbed in his work, meeting his comrades there in generous fellowship but his affections found intimate attachments in his family alone. Here he suffered the grievous loss of four of his children, one of them his son on whom his hopes were set. He underwent too the loss of his personal property during the inflation period besides bearing the burden of disappointment and anxiety concerning the existence and welfare of the institute. As an unwavering nationalist he suffered likewise keenly the pain of his country's disaster. He was not the man, however, to acknowledge defeat in his own plans, but renewed his courage with every fresh discouragement and exhorted his colleagues to follow with him undismayed toward their ends. Obstacles increased his resolution; with characteristic determination he could summon his strength and proceed with greater power through the difficulties toward his unrelinquished goal. He was an uncomplaining master of his fate, firm with himself and expecting others too to meet each his own lot. He was ready with help and advice when they were sought, but not eager to thrust them on others who should be left to master their own situations and meet their own problems.

Reserved, disciplined, conscientious toward his task, Kraepelin was not a man of narrow sympathies—far from it. Nor was he anything but a happy man. He found great contentment in his work and in himself. He had a healthy attitude toward disagreeable things, never

tarrying long with the thoughts of them once they had been met and dealt with as necessity demanded, and he was possessed of a readily functioning humor for difficult places.

A realist, one would say, and yet there was a Kraepelin dreamy, relaxed, yielding to nature's charm, of which we have already had glimpses, and, more, there was beneath the surface of devotion to duty, of persistence in a faithfully pursued aim, a conflict with the yearnings toward the other aspect of life. Even here there were two phases, the quiet satisfaction of yielding to peaceful delight and over against it the striving within of the craving for a vigorous activity which might fully take its own impulsive way. We know this not only from the confessions of the autobiographical material, but it is revealed more fully in his poems published after his death.

These poems, which were not written for publication, and were scarcely known during his life even by his friends, are a more spontaneous record than the autobiography of Kraepelin's inner self. The late Dr. J. Schwalbe, in reviewing these poems in the *Deutsche medizinische Wochenschrift*, of which he was the editor,[2] has said also of them:

> The conflict between the sacred spell of duty and the urgent longing for freedom, still more the realization of the *vanitas vanitatum*, of the limitation of all achievement, give rise to the disturbing sense of his own inadequacy and to a feeling of resignation, doubly affecting through its contrast with Kraepelin's great scientific accomplishments. That this note is most strongly and most frequently played upon is certainly not to be explained merely by the fact that most of the poems arose in the harsh autumn of life (1900-1916); there rings here the eternal cry of genius, which in its striving for the highest never finds perfection, which in its struggle for the unconditioned must always find its limitation in the borders of that which is humanly conditioned.

Kraepelin himself says of his poetry that comparatively late in life he began "to clothe certain moods and experiences in the form of emotional relations between the processes of nature and inner event." An ever-recurrent, almost despairing question of human destiny finds its counterpart in nature:

> Blue sea; a barren rock upspringing there,
> Defiant, hostile, scorched by the sun's outpour,
> A ceaseless haunting murmur fills the air,
> The song of billions on a desolate shore.
>
> The weary day departs in clouded red,
> And gray hangs heavy under frowning skies—
> The goal of all our living is to be dead?
> Or is our dying only that we'll rise?

2. Permission to publish this article as I wished was granted me by Dr. Schwalbe.

Or Kraepelin is aware that he wanders alone:

Strange am I here, acquainted with none;
Not a heart of another beats responsive to mine.
No one to ask of the way, whence comes it, where goes?

Or he is a prey to the discord within him, which after all he would not forego:

The torment of this discord who can tell?
How brims life's chalice oft with gall before me!
And yet, my deepest nature loves it well,
This rebel's strife! without it I abhor me.

There are joyous moods, sparkling with the vital motion of life itself, as when he pictures the stream that rushes down from its glacier cradle:

Merry is its play of youth;
See it sparkle, bubble, foam—
Dreams it darkly of a home
Striving toward a goal, forsooth?

Now, as if at call of fate,
Down it plunges to the deep,
Thundering, mighty in its leap,
Bent upon its way, elate!

White the spray from waters green,
Sheens of beauty tossing high,
Gay with color toward the sky,
Rainbows woven in the sheen.

And then in the Kraepelin who has been known as the rigidly earnest worker, carrying the burdens of a vast unfinished project, girding himself for fresh conflict with loss, disappointment and difficulty renew themselves. We find him withdrawing into the quietest moods of nature and resting dreamily in her arms:

I lie where woods are green,
Upon a bed of yielding moss
My grateful limbs reposing.
The sun's bright arrows dart across
My leafy screen, my eyes half closing,
I drift afar within the blue,
Where fleecy cloudlets softly glisten.
The murmur of the Isar, too,
Invites my drowsy ears to listen
The breeze plays gently, fans my brow,
The leaves for gossip its moment stealing.
A bird low warbles on a bough;
High up a hawk is wheeling.
A beetle trims itself for flight,
Its wings care-free extending;
I'll follow in my dreams own right,
To fairyland I'm tending.
I lie where woods are green.

A poem Kraepelin named "Autumn" I feel to be a brief portrayal of his life, its tasks permeated with longings, its boundaries yielding before his expanding spirit:

> I feel a gentle sorrow o'er me steal;
> It speaks of parting, of longings unfulfilled,
> Of wishes of the heart, desires unstilled,
> Of aims pursued with unrequited zeal.
> Yet while I dream thus, vanish time and space!
> The landscape fades away; I, too, am gone,
> All earth is from my reverent soul withdrawn;
> The riddle of eternity alone has place.

Kraepelin possessed a home which corresponded to some of his dreams, giving them fulfillment in an actuality in a softness and exuberance of nature. For many months of the year he retired to this estate on Lago Maggiore in northern Italy. Here he could work and rest and revel in the beauty which was at the same time reminiscent to him of lands beyond and of the rich heritage of history. It is significant that this estate, having been confiscated by the Italian government during the war, was afterward through the generous efforts of his Italian pupils and colleagues returned to Kraepelin in recognition of the great scientist, despite his sturdy German nationalism. It was chiefly through Mingazzini's persistent efforts that this happy return was brought about. Kraepelin enjoyed in this home a peaceful, simple life surrounded by the delights of mountain, lake and garden. The latter showed the master's own hand in its charming arrangement and in its rich collection of botanical rarities from all parts of the world, labeled with scientific care and exactness. Almost to the end of his life Kraepelin enjoyed here the active pleasures of bathing, rowing and mountain climbing. With his children he visited the highest peaks surrounding him and was not averse to spending the night in the open when no inn was at hand.

In addition to personal recollections of four visits to Kraepelin's villa, "Buon Rimedio," on the shore of Lago Maggiore, I here contribute a personal note from Dr. Meltzer on the occasion of a visit he made in August, 1927.[3]

> The eye roams enchanted from the large writing desk, which stands here today almost desolate and forsaken, out over the parapet of the balcony to the broad surface of Lago Maggiore, to the blue sunlit hills on the opposite shore, behind which Monte Motterone lifts its barren summit. How wonderful must be the view this bright August day there above looking upon the white peaks of Monte Rosa and Mischabel! Close by, only a mile or two before me in the lake, the Borromean Islands, the Isola Madre and the Isola Bella, with their tropical vegetation. But it is not only there that one may wander beneath the palms,

3. Meltzer: My Sojourn at the Villa Buon Rimedio: At the Same Time a Memorial to Kraepelin, Psychiat.-Neurol. Wchnschr. **29**:490, 1927.

of which two before the castle terrace of Isola Madre are the largest in Italy, as the guide has informed us; we need simply to step out upon the balcony of the villa Buon Rimedio to gaze upon palms, giant eucalyptus, camphor, magnolia, and tulip trees, upon native and exotic conifers. An enticing odor exhaled from blossoming oleanders, from roses and flowering borders, invites one to seek the secluded spots below in the garden with their massive stone tables and benches.

Just before one on the shore of the lake a vine-covered arbor, in which sat such a brief time ago the venerable master of German psychiatry, his eyes resting upon the variety of country about Lago Maggiore, which reminded him of the Grecian coast. In the east the Sasso di Ferro plunges into the green abyss of the lake; then the heights from Laveno on recede in lovely sinuous curves to the plains of Lombardy. And toward the west the snowy summits of the Simplon group across the Fondo Toce, behind which the rugged steeps crowd upon one another, scene upon scene. We walk further along the embankment and come to the harbor of the villa, in which a large rowboat lies rocking. He often rowed out from here upon the lake in the moonlight or refreshed himself bathing in its waves after a strenuous mountain trip. For he liked even in his last years to climb with his children to the highest peaks in the region round, even indeed in places where there were no inns, to spend the night in the simplest manner in some sheltered spot. We climb up to the large terrace which overhangs the harbor and from here we have an especially fine view of the villa Buon Rimedio, which strikes us as one of the most beautiful architecturally on the shore from Suna to the landing place in Pallanza.

It contains on the raised ground floor a dining room with a glass veranda, and adjoining it the kitchens and servants' quarters. In the first story the study, living room, library, and sleeping rooms of the family, in the second story three guest chambers. All of imposing dimensions. The magnificant stairway, which from the lake appears as a tower gracefully punctuated by its windows, ends at the top in a tower room from which one can look far out over the entire bay of Pallanza. Everything within the house is practically but simply arranged, in accordance with the owner's taste. The garden which surrounds the villa is laid out in masterly style. The water splashes through a faun's head into a basin under the cool shade of a paulownia tree. Close by it is a cool spot even in the hottest months of the year, from which one may obtain through the palms of the garden in front a view of the glittering lake. The mossy wall above the stone bench of this nook would be the most suitable place in which to erect a marble tablet upon which the *Deutsche Verein für Psychiatrie* (German Association for Psychiatry) might gratefully remember him who found here relaxation from his work and work in his recreation. His Italian pupils and colleagues were able while he still lived most beautifully to repay their debt to him by accomplishing through personal influence with the chief authorities the return of his property on the part of the Italian Government after the war.

We climb up between the faun grotto and the spot just mentioned by a stone stair to reach again a secluded resting place, which lifts itself like a pulpit over the place below. Kraepelin jokingly called this the throne of Philip II, because at one time nearly twenty years ago, when he had the garden laid out, he had a beautiful view from there of the latter's summer palace. Now it is veiled in a green twilight through the thick leafy covering of the trees whose branches have shot up, so that only the neighboring region can be seen. A few steps further and a bridge spans a small stream which flows under the street from the terraced garden on the other side and leaps down to the lake between yucca palms and an ivy-covered wall. Thick hedges of bamboo prevent the garden from being seen from the street, which leads behind the estate from the city of Pallanza to its

station on the Simplon railway. A eucalyptus tree which in just twenty years has grown beyond the ridge of the villa almost twenty-five meters high, casts its bark there annually every summer. We wander by it and come again through shady flowering arbored walks to the wall by the lake, in the mortises of which hedge roses have found their home, to delight us with their fragrant blooms. This garden planted here in the Occident is a paradise for the botanist, who will find in it rare plants from all parts of the world, beautifully labeled as in a botanical garden. They remind us at every turn of him who planted them here and who rejoiced in their growth.

It will soon be a year since his eyes closed forever. No longer than a year ago he dwelt here apparently well and hearty, diligently at work completing the last edition of his textbook, as if he had no time for weariness. Then came the day when his illness seized him and compelled him to leave his Buon Rimedio prematurely never to see it again. At this time the thought came to him whether it would be possible for his family to keep permanently this lovely estate here in Italy. He believed many of his colleagues, who, as he knew, lived for the most part in very straitened circumstances in these present conditions of reduced income and high costs, would doubtless be glad to know that there was a place here for as many as were not prohibited by the journey to Pallanza.

There lingers fresh and sweet in my memory a visit I made in 1924 to this same garden. Here again our botanical interests formed the chain of our talk. Kraepelin's collection of semi-tropical plants was extraordinarily rich and diversified. He was delighted in showing me and having me smell all of the odoriferous plants he had assembled. A never to be forgotten trip to Isola Bella rises before my eyes. It is a good stiff row to Isola Bella from Buon Rimedio, but Kraepelin manned the oars and with the help of a husky maid he rowed my wife and me to the Isola where he showed me its rich assortment of semi-tropical plants.

It was a memorable day. The proofs of his "General Paralysis" revision for the ninth edition were in his desk. The innumerable monographs and "separat Abdrücke" were there, and he was happy that it was finished. To Lange he had commissioned the opening volume. We spoke of our earlier contacts, our earlier friends, and as we took our way to Pallanza he accompanied us in the trolley and bade us Godspeed.

In this garden Kraepelin worked on the final edition of his textbook, when illness compelled him to leave his home, never to see it again. He left it in the hope not only that his family might keep the villa for their own use, but that numbers of his colleagues, under the straitened conditions of the time, might find there a place of occasional relaxation. Arrangements to that end have been made for accommodation available at any time of the year for such quiet among his fellow workers who might seek it.

Credit and thanks are hereby acknowledged and tendered to Louise Brink, Ph.D., who materially assisted in the preparation of this paper, particularly in the translation of the poetry.

HEAD INJURIES: EFFECTS AND THEIR APPRAISAL

I. EXPERIMENTAL STUDIES OF INDUCED CONVULSIONS AND VENTRICULAR DISTORTION IN THE CAT *

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HISTORICAL REVIEW

The rôle of head trauma in the production of convulsive phenomena is well known. Experimentally, this problem has received much attention. Brown-Séquard, in 1851, traumatized various parts of the central nervous system in rabbits and was able to induce convulsions by means of lesions of the medulla, cord, peduncles and quadrigeminal bodies. He observed that contralateral convulsive phenomena occurred secondary to cerebral lesions. Nothnagel, in 1868, produced small focal lesions in the pons in rabbits and also was able to elicit convulsions. Subsequently, Westphal (1871) was able to produce fits in rabbits by striking them on the head. The convulsions appeared directly or within a few seconds following the trauma and in some of these animals continued for several months. Later, Luciani (1878) and Vulpian (1885) were able to obtain spontaneous epilepsy in dogs and cats by the excision of various cortical areas. Convulsions did not appear immediately following these cerebral ablations, but developed several days, weeks or months after the injury, and the fits were observed to start on the side contralateral to the cerebral lesion. Goltz (1892) carried out extensive cerebral extirpations on dogs, and observed that his animals usually died in status epilepticus several months later.

Coincidentally, work by Morcé (1864), Magnan (1876), Victor Horsley (1885), Hughlings Jackson (1885), Ziehen (1886) and Abel and Barbour (1910) with the use of convulsant drugs and dyes was adding to the knowledge of the location and modification of convulsive phenomena. Barbour and Abel (1910) showed, in frogs, that following injury to the brain convulsions could easily be induced by cold, fatigue and subminimal convulsive doses of acid fuchsin. This work was confirmed by Thomas (1921). Abel (1912) first demonstrated, and Syz [1]

* Submitted for publication, July 13, 1931.

* From the Laboratory of Experimental Neurology, Department of Laboratories, Bellevue Hospital.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

1. Syz, J.: Acid Fuchsine and Brain Trauma in Frogs, J. Pharmacol. & Exper. Therap. **21**:263 (June) 1923.

(1923) confirmed the observation, that in the frog the injured central nervous system stained a deep pink after injections of acid fuchsin (in a quantity sufficient to cause convulsions), while the intact frog's brain remained uncolored by this dye in a similar concentration. Sauerback (1913), working on rabbits and monkeys, was able to show that following trauma to the motor cortex (by puncture, painting with iodine or the intracerebral implantation of foreign bodies) the animals could be given convulsions by one fifth of the convulsive dose of cocaine required for intact control animals. This increased susceptibility to convulsions caused by cocaine persisted for from two to eight months. Dandy and Elman [2] (1925) demonstrated in cats an increased susceptibility to convulsions induced by absinth for a period of from four to twenty weeks following various cerebral lesions. They believed that injury to the motor cortex causes greater sensitization to motor convulsive phenomena than do lesions of other cortical areas. This was confirmed by Pike [3] (1931), Muskens [4] (1928), me [5] (1930) and others.

Recent work by del Rio Hortega [6] (1927), Foerster [7] (1930) and Penfield [8] (1927 and 1930) has subsequently related the formation of a cerebral cicatrix and ventricular distortions to posttraumatic convulsive phenomena, and has devised a method for the surgical amelioration of this type of epilepsy.

EXPERIMENTAL PROCEDURES

In this study of injuries of the skull and brain the cat was used as the experimental animal. The reactions of animals with fractured skulls and postoperative cerebral scars were studied as regards both their behavior to a standardized convulsant (camphor monobromide) and the effects produced on the ventricular system of the brain following such procedures.

One series of animals was given aseptic cerebral lacerations of various areas of the brain. The technical procedure in this group was as follows: Under ether anesthesia, the hair over the skull was clipped and then entirely removed by a depilatory. The skin was painted with iodine and the scalp was incised, the temporal muscle retracted and the skull trephined over various regions. The dura was then punctured by a needle, or a small slit was made with a knife, and the

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2. Dandy, W. E., and Elman, R.: Studies in Experimental Epilepsy, Bull. Johns Hopkins Hosp. **36**:40 (Jan.) 1925.

3. Pike, F. H., et al.: Some Observations on Experimentally Produced Convulsions, Am. J. Psychiat. **10**:4 (Jan.) 1931.

4. Muskens, L. J. J.: Epilepsy, New York, William Wood & Company, 1928.

5. Wortis, S. B., and McCulloch, W. S.: Head Injuries: An Experimental Study, Arch. Surg., to be published.

6. del Rio Hortega, P., and Penfield, W.: Cerebral Cicatrix, Bull. Johns Hopkins Hosp. **41**:278 (Nov.) 1927.

7. Foerster, O., and Penfield, W.: The Structural Basis of Traumatic Epilepsy and Results of Radical Operation, Brain **53**:99, 1930.

8. Penfield, W.: The Mechanism of Cicatricial Contraction in the Brain, Brain **50**:499, 1927.

cortex directly underlying was traumatized (but not removed) to a depth of about 2 mm. over a surface area of from 2 to 3 sq. mm. Bleeding was controlled by cotton pledgets. The overlying muscle was then sutured in place and the closure of the scalp made with black silk sutures. The animal was observed for varying periods, and was subsequently given convulsions by the use of a standardized solution of camphor monobromide.

A second group of animals were subjected to skull fracture by being struck with a 1 pound hammer over the left frontoparietal area. The animal abruptly became limp, lost consciousness and momentarily stopped breathing, and in some instances died suddenly. The detailed observations will be described later.

In all the animals convulsions were produced at varying periods following cerebral laceration or fracture of the skull by means of the following technic. One or 2 cc. of 0.5 per cent solution of procaine hydrochloride was injected into Scarpa's triangle on the inner region of the thigh; the skin was incised and the femoral vein exposed. Gradually increasing quantities of a standardized solution of camphor monobromide were injected directly into the femoral vein at ten minute intervals. The solution was made by dissolving 10 Gm. of camphor monobromide, U. S. P., in 100 cc. of 95 per cent ethyl alcohol. In a group of normal control animals it required from 0.018 to 0.026 cc. of this solution per pound (0.5 Kg.) of cat to produce a severe generalized clonic convulsion. The method

TABLE 1.—*Convulsant Dose Following Laceration of the Brain in Cats*

	Number of Cats	Cc. Standard Convulsant per Pound of Cat		
		1 Day	4 Days	10 Days
Left motor cortex	5	0.024	0.024	0.018
Left parieto-occipital cortex	5	0.022	0.022	0.020
Left cerebellar cortex	5	0.022	0.022	0.020

has been described in detail in a previous publication.[9] The dose per pound of cat at which a general convulsion first occurred was taken as the minimal convulsive dose. A group of intact normal animals were convulsed at similar intervals and were used as controls.

After varying periods the animals were killed (with ether or chloroform), a solution of bromide-formaldehyde mixture was injected into the heart, the brain was removed, and the viscera were examined grossly. After fixation for from seven to ten days in a bromide-formaldehyde mixture, the specimens were sectioned and photographed, and in some cases studied microscopically. Gross evidence of fracture of the skull bone, meningeal thickenings, meningocerebral adhesions, lacerations of the brain and distortions of the ventricular system were noted. Complete histopathologic studies are at present under way. Dr. Lewis Stevenson, neuropathologist to Bellevue Hospital, will report some of the histopathologic observations.

OBSERVATIONS

Laceration of the Brain.—In a group of 15 cats, lacerations of the brain were made in the motor, parieto-occipital and cerebellar cortex as shown in table 1. The signs attributable to lesions of the brain in these

9. Wortis, S. B.; Coombs, H. C., and Pike, F. H.: Camphor Monobromide—A Standardized Convulsive Agent, Arch. Neurol. & Psychiat. **26**:156 (July) 1931.

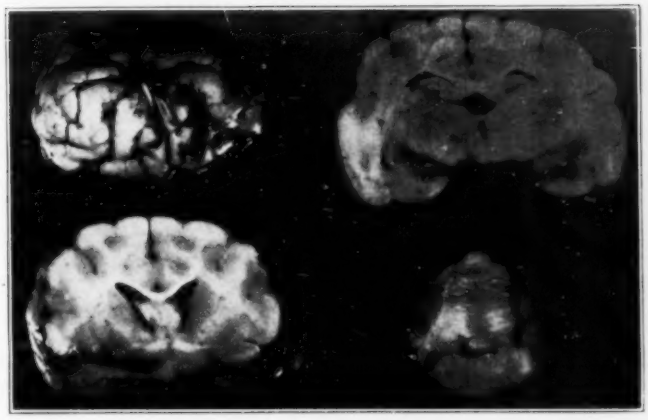

Fig. 1.—Specimen from the series in which fracture of the skull was produced. There is moderate bilateral ventricular dilatation.

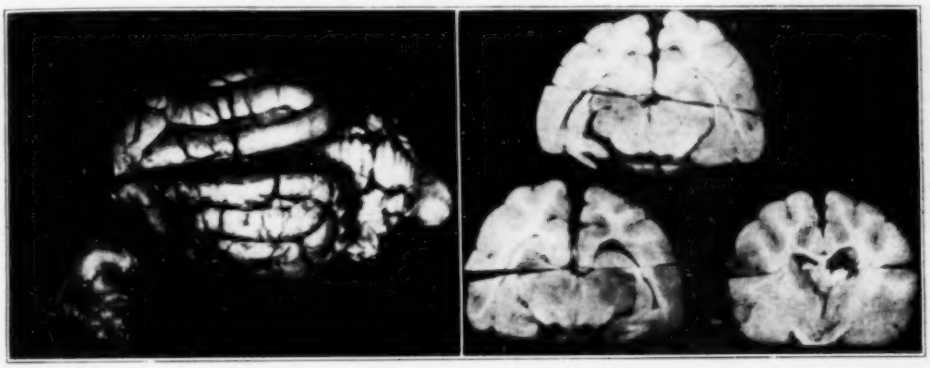

Fig. 2.—Extradural foreign body pressing into the left motor cortex. The entire ventricular system is pushed over toward the opposite side. The ipsolateral ventricle is collapsed; the contralateral ventricle is markedly dilated.

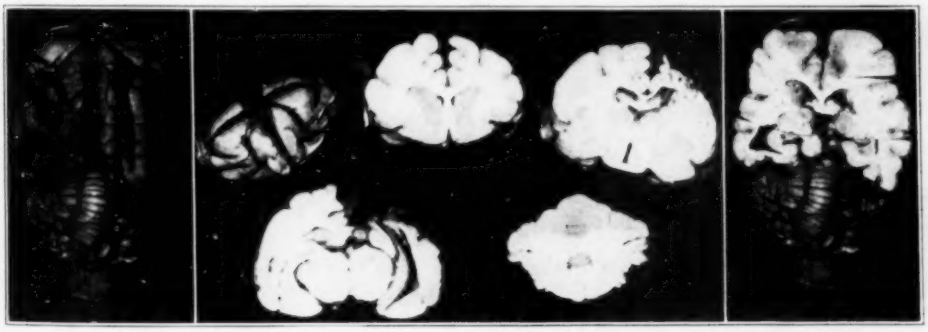

Fig. 3.—Lesion produced Oct. 10, 1930; specimen obtained Jan. 13, 1931, and photograph taken January 16. There is a meningocerebral scar over the left parieto-occipital cortex. The ventricle directly underneath is dilated and pulled up by the adherent scar.

areas were noted and have been described in a previous paper. The animals were convulsed at varying postoperative periods, and the increased sensitiveness of the traumatized area to camphor (and in some cases to absinthe) was demonstrated.

The most commonly found grossly visible postoperative cerebral lesions were:

1. Meningocerebral adhesions. This type of scarring was described by Penfield and evidently varies directly with the amount of injured cerebral tissue left behind.

2. Contracting cerebral cicatrix, with overgrowth of microglia cells early and fibroblasts and collagen fibers later. The details of the histopathology is described by Dr. Stevenson.

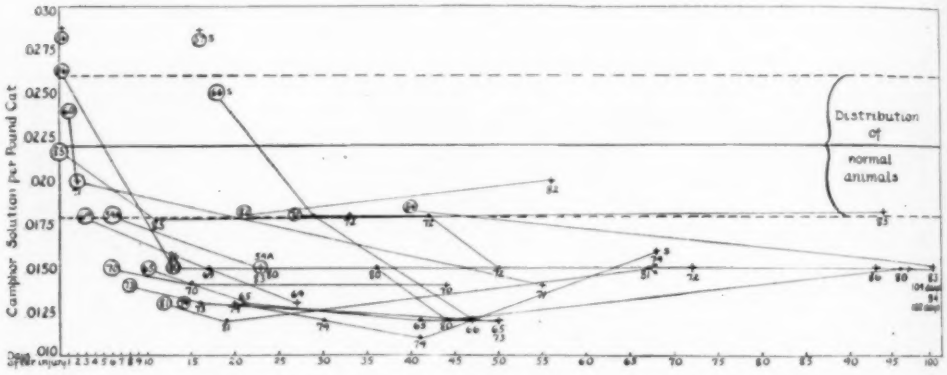

Chart showing distribution of animals with head injuries with reference to the minimal convulsive dose of camphor monobromide. *S* indicates a febrile animal; +, animal killed.

3. Ventricular distortion. The entire ventricular system is pulled toward the side of the lesion (scar), and there is often dilatation of the entire system (especially the first, second and third ventricles), which is especially marked on the side of the lesion. This confirms work by Penfield and Foerster who showed that "in experimental animals the brain at the site of the wound is pulled up through the operative bony defect by scar to the overlying muscle. That this is not due to simple brain edema is testified to by the passive enlargement of the underlying ventricle showing that the lateral wall is pulled away, not pushed out by the rest of the brain." This ventricular shift is especially interesting when compared with a series of ventricular pictures produced by extradural foreign bodies (comprising approximately 4 per cent of the intracranial cavity volume) pressing into the brain. In this series the ventricle on the side of the lesion is invariably found

slightly collapsed and pushed over toward the opposite side, and the contralateral ventricle is usually dilated.

Fracture of the Skull.—Twenty-four cats were subjected to fracture by the method described. The observations in this group are noted in table 2.

TABLE 2.—*Observations of Cats After Skull Fracture*

Cats with head trauma	24
Cats still living	7
At the time of injury	
Unconsciousness	18
Bleeding from orifices	17
Convulsions, tonic or clonic	11
Paresis (right side) noticeably lasting only 2 or 3 hours	11
Skull deformity discernible	3
Pupils—Equal and moderately dilated	14
R > L	2
L > R	8
Loss of sphincter control (bladder or bowel)	7
Gross postmortem observations in 17 specimens	
Skull fracture	
Linear	5
Depressed	2
Grossly normal	10
Brain	
Gross laceration	2
Hemorrhage into substance or over cortex	6
Adhesions (meningocerebral)	6
Blood in ventricular system (one marked hematocephalus)	4
Normal	2
Meninges	
Thickened (or adhesions)	7
Normal	10
Ventricles	
Slight to moderate general dilatation bilateral	6
Hematocephalus	1
Slight amount of blood in ventricle	3
Normal	7
Time distribution of results	
Died directly following trauma	4
Killed after convulsions (injections of camphor)	13
Distribution: 113 minutes and 6, 9, 17, 23, 35, 44, 50 (2 cases), 55, 56, 68 and 72 days	
Living	7
Total animals	24

The minimal convulsive dose of the standard camphor solution required immediately after injury is within or above normal limits, but within five days the dose falls and remains below normal limits, over the period noted in the chart.

COMMENT

Laceration of the brain with retention of the products of trauma results in meningocerebral adhesions and contracting cerebral cicatrix. This confirms the observations of del Rio Hortega [6] in cats, and of Foerster and Penfield [7] in dogs and rabbits. In this series there are no wounds in which the products of the trauma were removed, in which Penfield described neither cicatrix nor contraction. In the two aforementioned conditions, distortions of the ventricular system occur either

as generalized internal hydrocephalus, which was described by Bagley,[10] in 1927, as developing in dogs, and more readily in puppies, in which blood was introduced into the subarachnoid space. Bagley also accurately described meningeal reactions, and in prolonged cases structural changes in the underlying cortex usually associated with spontaneous convulsions. In cases with meningocerebral adhesions, in addition to the internal hydrocephalus, and in many cases as a solitary observation, dilatation of the ventricle directly underlying the scar and pulling over of the entire ventricular system toward the traumatized side were found.

The importance of this observation to clinical application was noted by Foerster, in 1924, who in his encephalographic studies on persons with brain wounds noticed a wandering of the ventricle to the side of the lesion. This was confirmed by R. Wartenburg, (1924) and later by P. Bielschowsky [11] 1928, who reported encephalographic observations in 106 cases following head trauma. Wilder Penfield showed experimentally that after a stab wound of the brain connective tissue filled the area and soon formed a resistant core attached to the meninges. He found that this core could be withdrawn like a thread from the track by lifting the meninges from the brain. The early microglial reaction, the later neuroglial astrocyte and the transition of microglia to compound granular corpuscles were noted by him.

Stenthal and Nagel studied more than 600 cases of gunshot wounds of the brain and found that 29 per cent of the patients subsequently had epilepsy. On the other hand, Villaret and Bailby reported an incidence of epilepsy of 7 per cent (in 500 cases), Collier from 5 to 8 per cent, and Reichman only 3.8 per cent (in more than 600 cases studied) with convulsive seizures. This wide variety of figures must undoubtedly be associated with a corresponding variety of lesions. The more severe cases of trauma of the brain undoubtedly give rise to a greater percentage of convulsive episodes and probably depend on whether or not extensive cerebral laceration occurred at the time of injury. Slight subarachnoid bleeding may temporarily sensitize the animal to noxious stimulation (physical, chemical, toxic or vascular).

The increased susceptibility of animals to camphor convulsions after head trauma is of great interest. Whether this is due to blood in the subarachnoid space or whether the trauma causes some physicochemical change in the reactibility of brain tissue to different noxious substances (as implied by Abel, Syz and Barbour) has yet to be determined. My

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10. Bagley, Charles: Functional and Organic Alterations Following the Introduction of Blood into the Cerebrospinal Fluid, Proc. A. Res. Nerv. & Ment. Dis. **8**:217, 1927.

11. Bielschowsky, P.: Disturbances of the Spinal Fluid System in Head Trauma, Ztschr. f. d. ges. Neurol. u. Psychiat. **117**:55 (Nov.) 1928.

associates and I are at present studying the effects of blood introduced into the subarachnoid space (with minimal trauma) on the convulsive dose of camphor, in an attempt to analyze further these experimental data.

CONCLUSIONS

1. Aseptic laceration of the brain without removal of the products of trauma, in the cat results in ventricular distortion due to: (*a*) meningocerebral adhesions, and (*b*) contracting cerebral cicatrix.

2. Head trauma resulting in the escape of blood into the cerebrospinal fluid often gives rise to mild bilateral ventricular dilatation in the absence of grossly demonstrable meningocerebral adhesions or a cerebral scar.

3. Aseptic laceration of the brain and head trauma resulting in fracture of the skull increase the animal's sensitiveness to a standard convulsant over the period of observation.

HEAD INJURIES: EFFECTS AND THEIR APPRAISAL

II. THE RÔLE OF THE MICROGLIA *

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The manner in which the microglia cells react in cases of injury to the brain was first brought to my attention by Hortega in 1926. He had perfected a stain for the demonstration of microglia and had shown by its use the life history of these mesodermal cells, which have been called the "third element" in the nervous system.[1]

In Hortega's drawing (fig. 1), one sees the microglia cells appearing in the brain about the time of birth in the form of rounded cells. These cells soon acquire small buds or processes, and, as they migrate to their final positions in the nervous system, they gradually acquire the long, thin, spiky processes that enable one to distinguish them from all other cells in the nervous system when properly stained by Hortega's method.

In the case of an injury to the brain, the microglia cells undergo a change that is just the reverse of the changes shown in their development. The processes become swollen and shorter, and the cell body gets larger and rounder. The cells become actively motile and phagocytic, and move up in countless numbers to the site of the injury, multiplying by mitosis on the way. When they have arrived at the lesion, the cells begin to devour the broken down brain tissue and the other products of the injury and are now easily demonstrable as fat granular corpuscles with sudan III or other fat stains, or, indeed, with ordinary aniline dyes. As the name implies, they are now loaded with fatty substances, which they remove to the blood vessels of the contiguous areas. This process has already been demonstrated by Hortega and Penfield [2] and others, but it will bear mention again here because it is not yet fully appreciated by many.

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* Submitted for publication, July 13, 1931.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

1. del Rio-Hortega, P.: Histogénesis y evolución normal; Exodo y distribución regional de la microglia, Mem. r. Soc. españ. de hist. nat., 1921, vol. 11.

2. del Rio-Hortega, P. and Penfield, Wilder: Cerebral Cicatrix, Bull. Johns Hopkins Hosp. **41**:278 (Nov.) 1927.

The particular point that I wish to stress in this paper is the disappearance of brain tissue that results from this eating-up activity of the microglia. It seems possible that the cells devour more of the brain than is necessary from the observations I have been able to make, not only on the brains of experimental animals, but also on human brains which have been injured on one side and which it has been possible to visualize during life by means of encephalography or ventriculography.

Encephalograms of patients who have been injured on one side of the brain show, on the injured side, the lateral ventricle very much

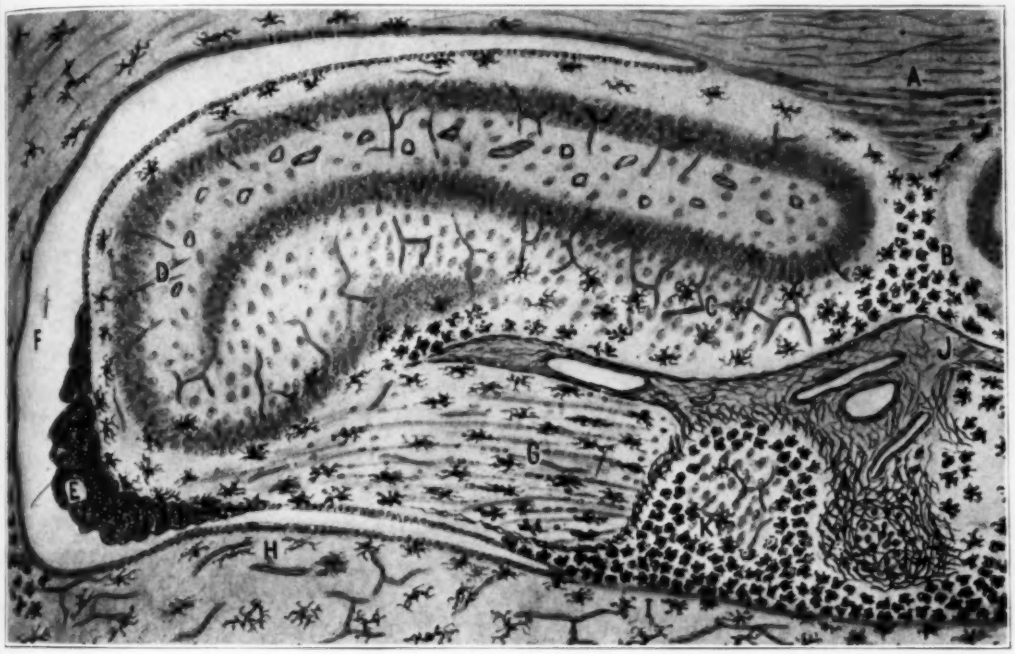

Fig. 1.—Hortega's drawing of the appearance of the microglia in the brain of a rabbit 4 days old, and their original appearance in the form of rounded cells which change their shape as they travel away to their final destination in the brain. *A* indicates the corpus callosum; *B*, Ammon's fissure with globulous microglia; *C*, microglia emigrating to the cornu ammonis; *D*, the hippocampus; *E*, the choroid plexus; *F*, the lateral ventricle; *G*, the fimbria; *H* and *I*, the optic thalamus; *J*, the tegmen ventriculi quarti; *K*, the nucleus habenulae.

larger than on the normal side. Often the ventricle on the injured side not only is larger than normal, but may be pulled over to the injured side by adhesions and contraction of the scar formed at the surface of the brain, as Penfield has shown. For the most part, however, it

Fig. 2.—Microglia as they appear in a normal cat's brain, stained by Hortega's silver carbonate method.

seems that this loss of substance, represented by the increase in the size of the ventricle, is due to the phagocytic action of the microglia.

Figures 2, 3, 4 and 5 show the normal microglia in a cat's brain, and the changes that occur in them when the brain has been injured by an aseptic puncture of the cortex and stained for microglia at different lengths of time following the operations.

Fig. 3.—A low power photomicrograph of the whole lesion produced by a stab wound of a cat's brain. The animal was killed ninety-five hours after the operation, and the brain was stained as before for microglia. Hundreds of these cells can be seen about the margin of the injured area in the form of rounded black dots.

One may conclude from these preparations that injury to the brain is not always as harmless as one is sometimes apt to think. For example, after a needle puncture of the brain during an operation, one may be sure that the microglia react in this way, and it is hard to tell just where their activity will end and with how much loss of brain tissue.

From this point of view the matter has a medicolegal aspect of some importance. Undoubtedly, some of the cases following brain trauma that have been classified as instances of neuroses show a train of symptoms that is not dependent on a desire for compensation but is due to the phagocytic action of the microglia with its attendant phenomena. At least, in such a case of suspected neurosis, the patient is entitled not

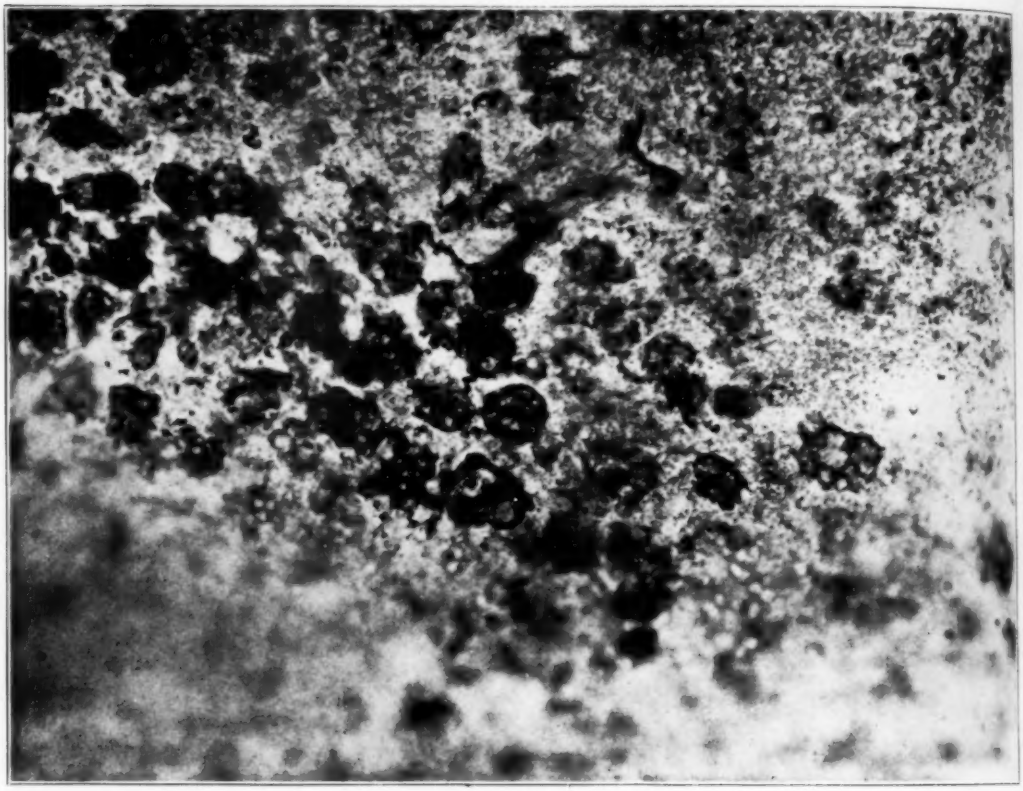

Fig. 4.—A high power photomicrograph of some of the microglia cells seen in figure 3. They can be seen here as definite compound granular corpuscles, but here and there they still possess a few of the processes of the normal microglia cells.

only to a roentgen examination of the skull, but also to an encephalogram.

Another important question, which cannot be fully answered by the present incomplete studies, is whether, in view of these facts, it would not be better to operate in more cases of skull fracture in which brain injury has taken place in order to remove any damaged areas of the

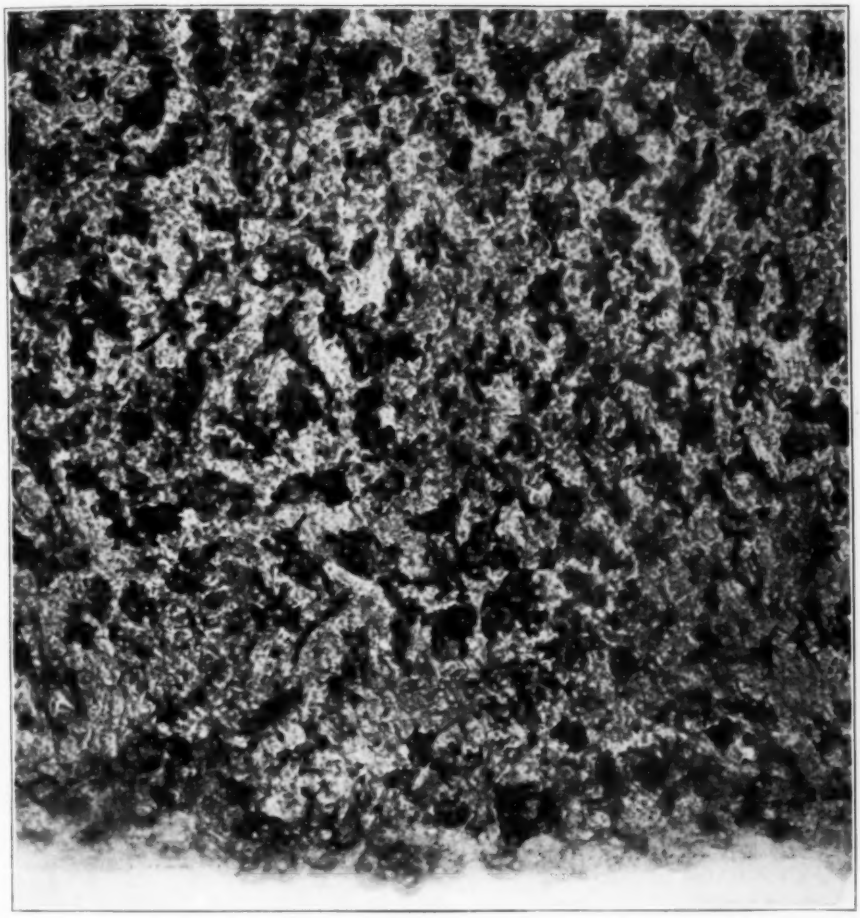

Fig. 5.—A high power photomicrograph of the microglia cells at the margin of a wound in a cat's brain. The animal was killed seven days after the operation, and the brain was stained for microglia. The transformation of microglia with processes into compound granular corpuscles without processes can be partly seen in this picture.

brain, thus diminishing, if possible, the phagocytic inroads of the microglia and the subsequent scars formed by the astrocytes.

After the microglia have devoured the tissue débris, indeed, while this is still in progress, the astrocytes begin to change in the contiguous areas; they multiply amitotically and form at last a dense scar composed of neuroglia cells with strongly developed fibers. Each astrocyte sends out one or more of these fibers, each with a sucker foot at its extremity by which it attaches itself to a blood vessel or to the under surface of the pia near the injury.

410 East Fifty-Seventh Street.

HEAD INJURIES: EFFECTS AND THEIR APPRAISAL

III. ENCEPHALOGRAPHIC OBSERVATIONS *

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This communication is based on a study of twenty cases of skull injury, four previously reported and sixteen comprising the present series.

Foerster,[1] Wartenberg [2] and especially Schwab [3] were the first to demonstrate abnormal encephalographic conditions in patients who had sustained skull injuries. Later, Heidrich,[4] Bielschowsky,[5] Pancoast and Fay,[6] Foerster and Penfield,[7] Frazier and others reported similar observations. In a paper on encephalography I included four cases of the posttraumatic state with abnormalities in the encephalogram.[8] Since then I have had the opportunity of observing sixteen additional cases of skull injury, the encephalographic conditions in which are reported in this communication.

REPORT OF CASES

CASE 1.—*History.*—Charles E. H., aged 39, a construction worker, was admitted to Bellevue Hospital on Nov. 21, 1929, complaining of pain in the back, headache and attacks of unconsciousness for one year. The previous and family histories were without significance. On Oct. 3, 1928, the patient was struck on the back of the head by a portion of a wall which fell 18 feet. He was rendered unconscious and was admitted in this state to Flower Hospital, where he remained for three days. There was bleeding from both ears and the nose. Spinal puncture showed clear colorless fluid, under a pressure of 14 mm. of mercury. Roentgen examination of the skull gave negative results. The clinical diagnosis was concussion of brain.

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* From the Neurological Service of Bellevue Hospital.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

1. Foerster, O.: Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:512, 1925.

2. Wartenberg, R.: Arch. f. Psychiat. **77**:507, 1926; Ztschr. f. d. ges. Neurol. u. Psychiat. **94**:585, 1925.

3. Schwab, O.: Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:294, 1926.

4. Heidrich, L.: Ergebn. d. Chir. u. Orthop. **20**:156, 1927; Beitr. z. klin. Chir. **137**:623, 1927.

5. Bielschowsky, P.: Ztschr. f. d. ges. Neurol. u. Psychiat. **117**:55, 1928.

6. Pancoast, H. K., and Fay, T.: Radiology **15**:173, 1930.

7. Foerster, O., and Penfield, W.: Brain **53**:99, 1930.

8. Friedman, E. D.: Further Experiences with Encephalography, Internat. Clin. **1**:53, 1930.

The patient returned to work on November 4, but four days later had a sudden spell of generalized rigidity. There were a number of similar attacks later on. Soon after the injury he also began to have attacks of pain in the back of the head, preceded by the seeing of sparks and a feeling of "pins and needles" in the feet. The attacks varied in duration from several hours to two or three days. He was often unconscious for hours, and felt tired and sleepy after the spells; there was no history of biting the tongue or of incontinence, but there had been occasional jerking of the left leg. At times there was a reddish discharge from the right ear.

He was observed at Mount Sinai Hospital in January, 1929 (four months after he had sustained the trauma). The chief complaints at that time were tinnitus in the right ear and attacks of vertigo. Physical examination revealed diminution of hearing on the right, but normal caloric responses. Local examination of the ear

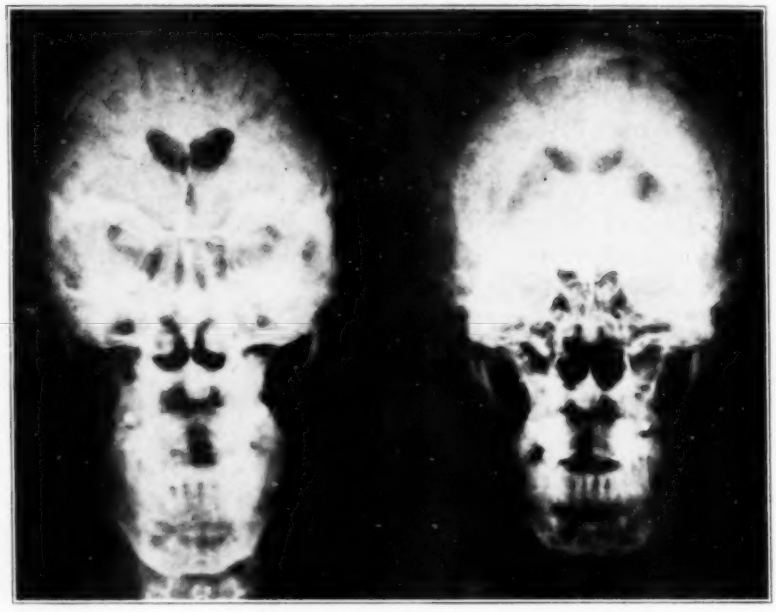

Fig. 1 (case 1).—Encephalogram, showing distention of the ventricles and a considerable accumulation of air over the convexity of the brain.

gave negative results; spinal puncture showed a clear fluid, under a normal pressure (160 mm.). Serologic studies gave negative results.

Examination.—Neural examination revealed no abnormalities; there was no evidence of a focal disease. A hyperpnea test proved negative. The case was classified as posttraumatic epilepsy.

Encephalography.—This procedure was carried out on Nov. 26, 1929, when 110 cc. of air was injected. The encephalogram revealed the presence of a considerable internal and a moderate external hydrocephalus.

Case 2.—George F., aged 22, a mover of furniture, was admitted to Bellevue Hospital on Oct. 28, 1929, complaining of nervousness, "shaking" and spells of unconsciousness. The family and previous histories were without significance. In

June, 1929, the patient was injured in an automobile accident, a car in which he was riding being overturned. He sustained a fracture of the skull and a fracture of the clavicle. He was removed to Nassau Hospital, Mineola, Long Island, where he remained for two weeks. Since then, he had had epileptiform seizures, associated with loss of consciousness, memory defects and personality changes (depression).

Physical Examination.—The neural status was normal, except for slight right lower facial weakness. The spinal fluid was normal. The Wassermann reaction of the blood was negative. Roentgen examination of the skull revealed a fracture of the left half of the occipital bone; there was no depression.

Clinical Diagnosis.—The diagnosis was posttraumatic epilepsy, with mental changes.

Encephalography.—This procedure was carried out on November 5, when 110 cc. of air was injected. The encephalogram showed a normal ventricular system, but a considerable accumulation of air over the convexity of the brain.

Case 3.—John S., aged 41, a laborer, was admitted to Bellevue Hospital on Feb. 11, 1930, complaining of headache, dizziness, loss of hearing on the right and pain in the right knee. The family and previous histories were without significance. On Dec. 19, 1920, he was struck on the right side of the head by a piece of falling iron. He sustained a scalp wound; he "felt very weak" and was brought to Bellevue Hospital, where he remained for two days. Immediately after the accident he noted loss of hearing on the right and dizziness. Since then, headache and dizziness had occurred with increasing frequency.

Physical Examination.—There were sluggish and unequal pupils; poor convergence; an absence of ankle jerks; nerve deafness on the right, with lateralization of the Weber test to the left, and some impairment of associated automatic movements of the left upper extremity. The otologist reported complete loss of hearing on the right, and normal hearing on the left; the vestibular reactions were normal; there was no discharge from either ear. The Wassermann reaction of the blood was negative. The spinal fluid was completely normal.

Clinical Diagnosis.—The diagnosis was old fracture of the right petrous bone, with postconcussion state.

Encephalography.—This procedure was carried out on Feb. 26, 1930, 90 cc. of air being injected. The encephalogram showed the presence of a low grade internal and external hydrocephalus.

Case 4.—Julius M., aged 20, an errand boy, was admitted to Bellevue Hospital on March 10, 1930, complaining of attacks of epilepsy. The family and previous histories were without significance. In 1920, the patient sustained a fracture of the skull from a fall. He was unconscious for several hours, and was operated on at Fordham Hospital. There was some residual bone absorption in the left occipital region. Five years later, he had the first convulsive seizure. The seizures recurred at intervals of about three months; they were ushered in by jacksonian twitchings on the right and a visual hallucination (the seeing of a white ball); the convulsion then became generalized, and there was occasional incontinence of urine.

Physical Examination.—There were diminution of the abdominal reflexes on the right, increased deep reflexes on the right and a depression in the skull on the left posteriorly. The spinal fluid was normal. The Wassermann reaction of the blood was negative.

Clinical Diagnosis.—The diagnosis was posttraumatic epilepsy on the basis of a meningocerebral scar.

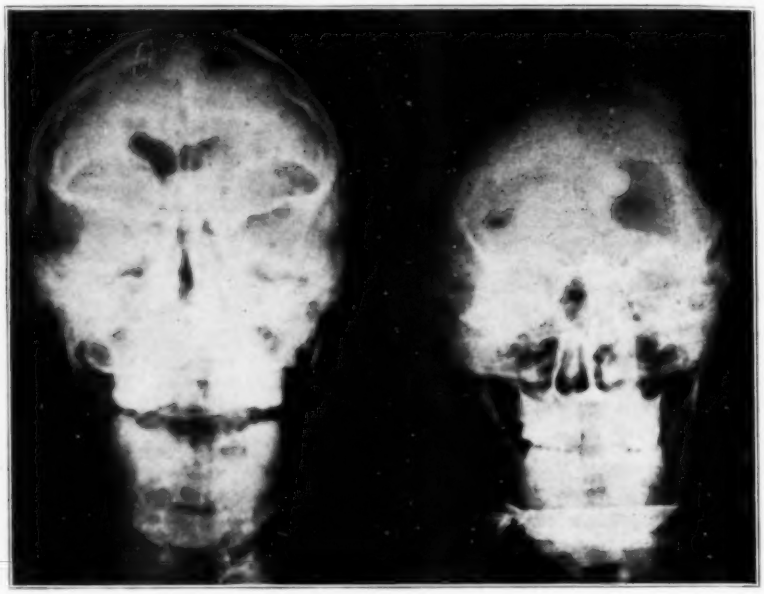

Fig. 2 (case 4).—Encephalogram, showing an asymmetric internal hydrocephalus with greater ventricular distention on the side of the lesion and migration of the ventricle toward the site of fracture.

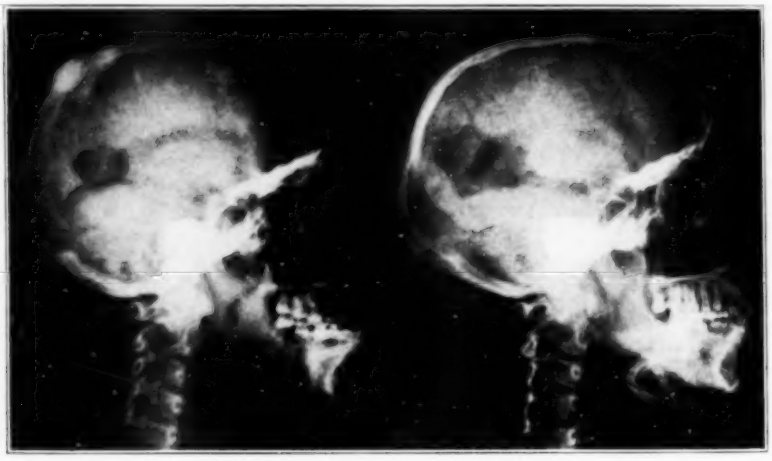

Fig. 3 (case 4).—Lateral view, showing the site of fracture, enlargement of the ventricle on one side and increased surface markings.

Encephalography.—This procedure was carried out on March 12, 1930, 145 cc. of air being injected. The encephalogram revealed considerable internal hydrocephalus, which was more pronounced on the left, slight external hydrocephalus and ventricular migration toward the site of the lesion.

CASE 5.—John M., aged 47, an elevator operator, was admitted to Bellevue Hospital on Dec. 30, 1930, with the complaint of irrationality following an automobile accident three weeks prior to admission ("talks silly"). The family history was without significance. The patient had had pneumonia two years prior to admission, with recurrent attacks of pleurisy. The chest had been tapped several times. He was the subject of moderate alcoholism.

On Dec. 9, 1930, while crossing the street, the patient was struck by an automobile; he was thrown down, and the back of his head struck against the curb; he was unconscious for over twenty-four hours, and was taken to Columbus Hospital, where he remained until December 30. When he regained consciousness, he was disoriented and had to be restrained. He thought that he was in the hospital for a cold; he had to be fed by tube for one week after the injury.

Physical Examination.—There were dulness and diminished breathing over the right side of the chest, probably due to a thickened pleura. Neural examination showed slight weakness on the left, left facial asymmetry, deviation of the tongue to the left, exaggeration of the deep reflexes on the left and a suggestion of a Babinski sign. The patient was disoriented and confused. Vestibular tests gave normal responses. The spinal fluid was under a pressure of 90 mm., and was clear, colorless and entirely normal. The Wassermann reaction of the blood and spinal fluid was negative. There was no roentgenologic evidence of fracture of the skull.

Clinical Diagnosis.—The diagnosis was intracranial injury involving the right hemisphere.

Encephalography.—This procedure was carried out on Jan. 12, 1931, 100 cc. of air being injected. The encephalogram showed a mild internal and external hydrocephalus.

Comment.—It is of interest that within a month after the patient sustained the injury the encephalogram already revealed deviations from the normal.

CASE 6.—John G., aged 49, a waiter, was admitted to Bellevue Hospital on July 15, 1930, complaining of headaches and nervousness for two years. The family and previous histories were without significance. The patient was injured in a railroad accident in July, 1928; he bled from both ears, and was unconscious for three hours. He was told by a physician that he had sustained a fracture at the base of the skull. He remained in bed for four weeks; he had not worked up to the date of admission. Since the accident, he had suffered from nervousness, palpitation, irritability and throbbing headaches. He expressed a morbid fear of insanity, and had mild paranoid notions and auditory hallucinations.

Physical Examination.—The neural status was normal, except for slight nerve deafness, which was more pronounced on the right, and overactive knee jerks. The spinal fluid was clear, colorless, and under a pressure of 360 mm. (the reading was made with the patient in the sitting position). Serologic studies proved negative.

Clinical Diagnosis.—The diagnosis was fracture at the base of the skull.

Encephalography.—This procedure was carried out on July 21, 1930, 100 cc. of air being injected. The encephalogram showed a low grade internal hydrocephalus, with a large accumulation of air on the surface of the brain.

Case 7.—Emil M., aged 34, a laborer, was admitted to Bellevue Hospital on July 31, 1930, complaining of pain in the head, dizziness and nervousness for the previous eight months. The family history was without significance. The patient had had influenza in 1919. On Nov. 13, 1929, he was struck on the head by a crowbar; he was unconscious for a few minutes, and sustained a laceration of the scalp; there was no bleeding from the ears or nose. Several hours after the accident, he had a chill lasting one hour; he vomited three or four times; he remained in bed at home for three weeks. Owing to continued dizziness, he sought medical advice. He had been unable to work since the accident owing to dizziness, trembling, weakness and faintness.

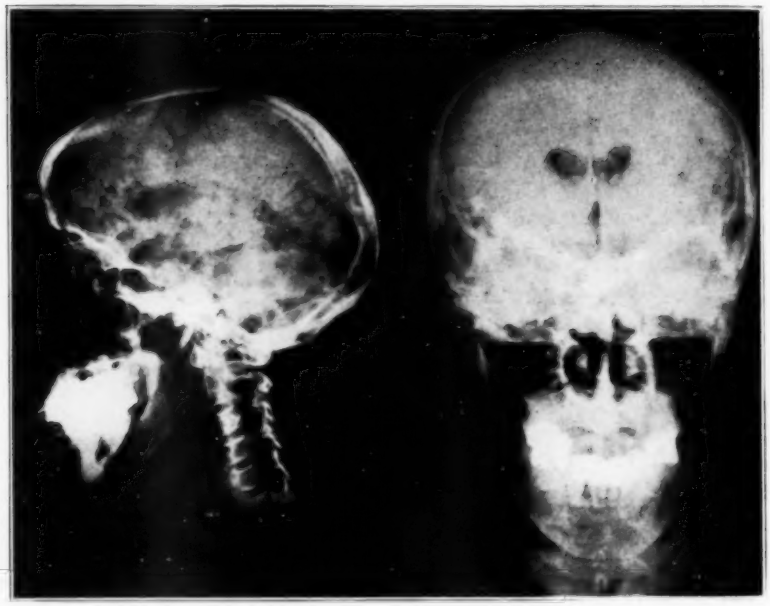

Fig. 4 (case 6).—Encephalogram, revealing the presence of a low grade internal and external hydrocephalus.

Physical Examination.—There were a right lower facial weakness, absent abdominal reflexes and increased deep reflexes. Vestibular tests gave normal responses. The spinal fluid pressure was 150 mm.; otherwise, the fluid was normal.

Clinical Diagnosis.—The diagnosis was postconcussion state.

Encephalography.—This procedure was carried out on Aug. 2, 1930, 105 cc. of air being injected. The encephalogram revealed a low grade of internal hydrocephalus.

Case 8.—William McP., aged 26, a laborer, was admitted to Bellevue Hospital on Nov. 24, 1930, complaining of "fits" for one year. The family and previous histories were without significance. On Dec. 24, 1929, the patient was struck on the head in the left frontoparietal zone. He was taken to a hospital, where he remained for two months. While there he developed convulsive seizures. The attacks began with trembling of the right arm; the convulsions later became gener-

alized and were accompanied by loss of consciousness, biting of the tongue and incontinence of urine. The number of attacks varied from one to five daily. Since the injury the patient had had little use of the right arm.

Physical Examination.—There were weakness of the right arm, no difficulty in speech (the patient was right-handed) and hyperactive biceps and triceps jerks on the right. The abdominal reflexes were not obtained on the right; all other deep reflexes were diminished. There was no Babinski sign. The blood pressure was

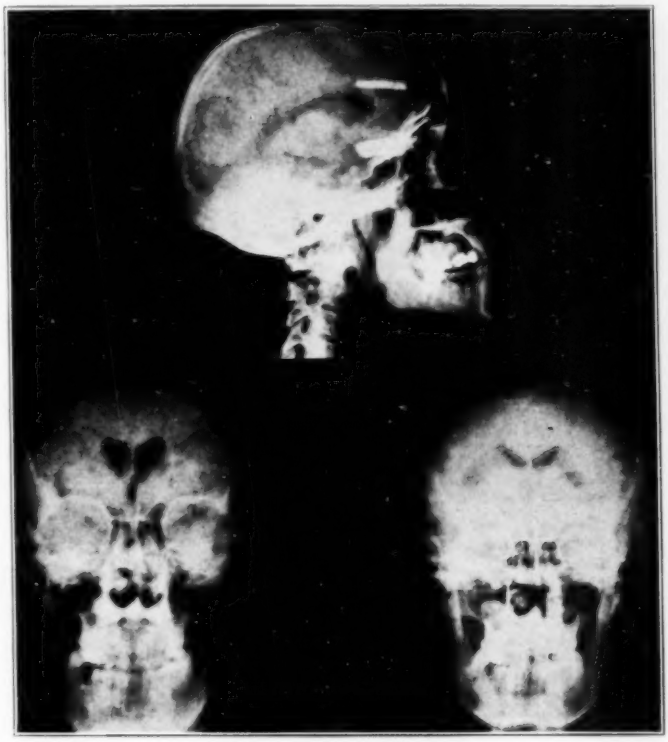

Fig. 5 (case 7).—Encephalogram, revealing the presence of a moderate symmetric internal hydrocephalus.

130 systolic and 90 diastolic. The Wassermann reaction of the blood was 4 plus. The spinal fluid was clear and colorless; the pressure was 140 mm.; the Wassermann reaction was negative; the colloidal gold curve was normal; there was no increase in cells or globulin. Roentgen examination of the skull revealed an area of rarefaction in the left parietal bone and an area of sclerosis just below it.

Clinical Diagnosis.—The diagnosis was depressed fracture; posttraumatic jacksonian epilepsy, probably due to a cortical scar with adhesions, and syphilis.

Encephalography.—This procedure was carried out on Dec. 18, 1930, 90 cc. of air being injected. The encephalogram revealed a dilatation of the ventricle on the left and a considerable accumulation of air over the surface of the brain. There was also some ventricular migration to the left and upward.

Comment.—The coincidence of syphilis and trauma is not unusual. A skull injury will frequently aggravate or make manifest a hitherto latent syphilis. The clear history and the objective evidence of skull injury in this case, however, make the traumatic genesis of the lesion the dominant factor in the case.

Case 9.—Arthur H., aged 43, a watchman, was admitted to Bellevue Hospital on Oct. 2, 1930, complaining of weakness of the left side following an operation for a skull injury, eleven years prior to admission, and left-sided convulsions for two and a half years preceding admission. The family history was without significance. Eleven years prior to admission, the patient was struck on the right side of

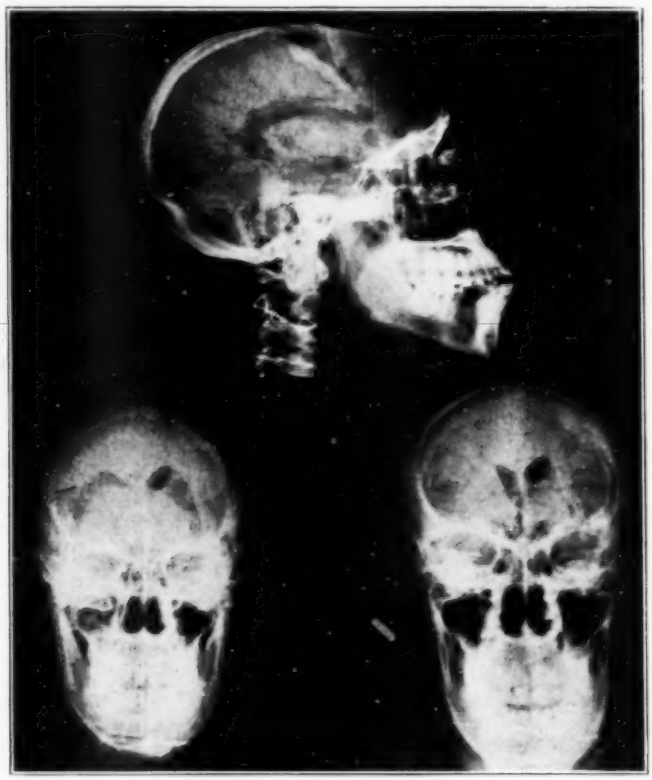

Fig. 6 (case 8).—Encephalogram, showing the presence of an asymmetric internal hydrocephalus with migration of the ventricular system toward the site of fracture.

the head and sustained a depressed fracture of the skull. An operation was performed at the Boston City Hospital; it was followed by paralysis of the left side of the body and impairment of hearing on the left. Motor power gradually returned, and the patient was able to make some use of the left arm and leg; he had more difficulty with the upper than with the lower limb. Two and a half years prior to admission, left-sided twitchings began; they occurred about once a month and continued for periods varying from three to four hours; at times they were associated with loss of consciousness.

Physical Examination.—There was a large bone defect over the right frontoparietal zone. The ocular fundi were normal. There were: left hemiparesis, increased deep reflexes on the left, an equivocal plantar response on the left and mild sensory disturbances with astereognosis on the left. The spinal fluid was entirely normal.

Clinical Diagnosis.—The diagnosis was traumatic epilepsy (probably due to a cortical scar in the right frontoparietal zone); residual hemiparesis.

Encephalography.—This procedure was carried out on Oct. 15, 1930, 90 cc. of air being injected. The encephalogram showed considerable internal hydrocephalus, which was more pronounced on the right, with ventricular migration toward the scar.

Following encephalography the patient improved: the attacks became less frequent.

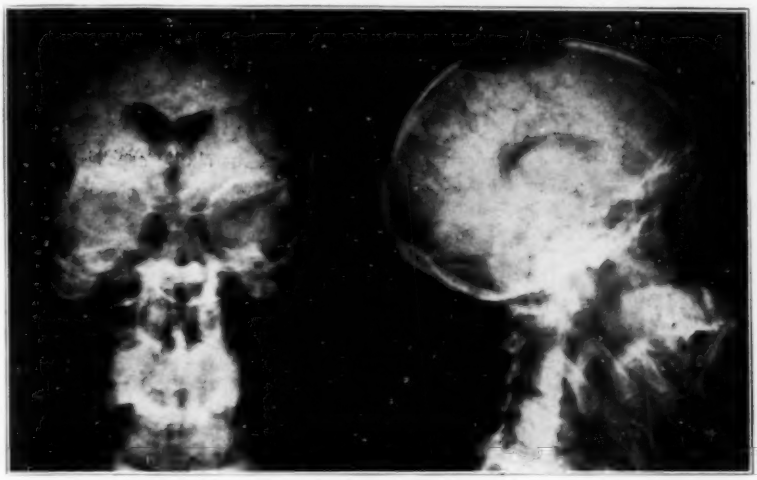

Fig. 7 (case 9).—Anteroposterior and lateral views, showing the presence of an asymmetric internal hydrocephalus with migration of the ventricular system toward the site of fracture.

Case 10.—Henry F., aged 27, a carpenter, was admitted to Bellevue Hospital on May 12, 1930, complaining of spells of loss of consciousness. The family and previous histories were without significance. Four years prior to admission, the patient was thrown from a motorcycle, and sustained a fracture of the skull. He recalled getting up on his feet immediately after the accident and being taken to St. John's Hospital, Long Island City. He subsequently lost consciousness and remembered nothing until two or three weeks later. He had been told that several pieces of bone had been removed from the site of the fracture. Two years later, he had a first petit mal seizure; these episodes recurred about once a month. At times there were convulsive movements in the arms and legs, and occasionally he bit his tongue.

Physical Examination.—There were somewhat sluggish pupils and hyperactive deep reflexes in the lower limbs, with ankle clonus and a Babinski sign on the right. The spinal fluid was normal. The Wassermann reaction of the blood was negative; the blood pressure was 130 systolic and 70 diastolic.

Clinical Diagnosis.—The diagnosis was posttraumatic epilepsy.

Encephalography.—This procedure was carried out on May 20, 1930, 90 cc. of air being injected. The encephalogram revealed a low grade internal and external hydrocephalus, which was more pronounced on the left.

CASE 11.—Charles T., aged 44, a tailor, was first admitted to Bellevue Hospital on Feb. 18, 1930, following an accident. While crossing the street he was struck by an automobile and rendered unconscious. He left the hospital on the same day at his own request. On February 22, he was seen by his family physician, who found him suffering from severe headache and exhibiting a definite bradycardia (the pulse rate was 52). He was readmitted on the same day, when his chief complaint was "terrible bad headache." The family and previous histories were without significance.

Physical Examination.—There was a laceration of the scalp in the left temporal region. The patient had occasional vomiting; there was no bleeding from the ears, nose or mouth. There were diminished abdominal reflexes and increased deep reflexes, but no Babinski sign. The fundi were normal. The blood pressure was 110 systolic and 60 diastolic. The spinal fluid was under normal pressure; the fluid was xanthochromic in all tubes. Roentgen examination of the skull and serologic studies gave normal results. The patient remained in the hospital until March 4.

Clinical Diagnosis.—The diagnosis was fracture of the skull; cerebral contusion, and subarachnoid bleeding.

First Encephalography.—This procedure was carried out on Feb. 26, 1930, 80 cc. of air being injected. The encephalogram showed normal ventricles.

Course.—Following the encephalography, the headaches disappeared. The patient was advised to return later for further encephalographic studies, and was readmitted to the hospital on June 13, 1930; he was discharged on June 24. Since discharge, he had complained of headache and fatigability.

Physical examination at this admission gave negative results. The blood pressure was 130 systolic and 90 diastolic.

Second Encephalography.—This procedure was carried out on June 17, 1930, 90 cc. of air being injected. The encephalogram revealed a low grade of internal hydrocephalus.

Comment.—It is interesting that the first encephalogram (one week after the injury) showed no deviation from the normal. The second (four months later), however, showed a definite abnormality. Evidently the reparative process had so altered the brain tissue as to give rise to the changes noted.

CASE 12.—John M., aged 39, a laborer, was admitted to Bellevue Hospital on Feb. 23, 1931, complaining of left-sided headache, throbbing in the left ear, visual disturbances in the left eye and dizziness. The family and previous histories were without significance. On Nov. 29, 1927, the patient was struck on the head by a heavy piece of iron; he was unconscious for half an hour, and was taken to the Knickerbocker Hospital, where he remained for one month. There was no bleeding from the nose, ears or mouth. There was nausea, but no vomiting. Roentgen examination of the skull gave negative results. The patient was discharged with a diagnosis of laceration of the scalp and cerebral concussion. Since then he had complained of the symptoms noted.

Physical Examination.—The pupils were unequal (the right larger than the left), but responded well to light and in accommodation. Taste and smell were impaired. There were left-sided sensory disturbances (especially of the pain and temperature sense), but the corneal reflex was normal; the blood pressure was 106 systolic

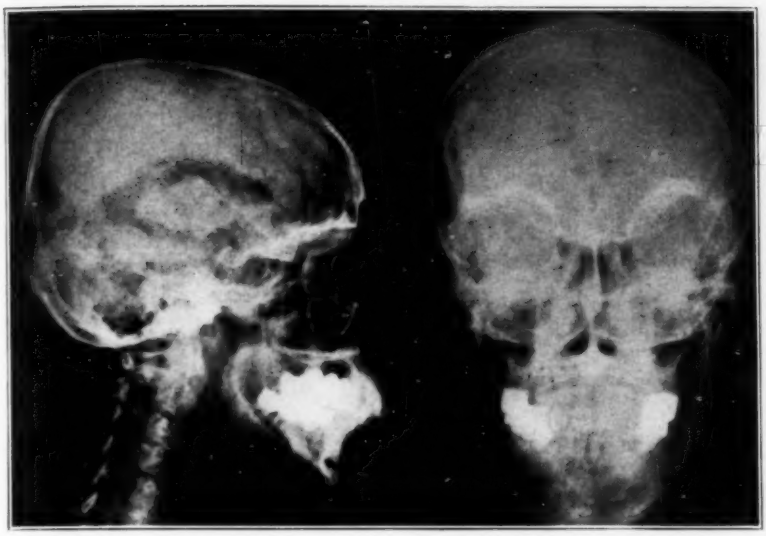

Fig. 8 (case 11).—Encephalogram, revealing normal characteristics.

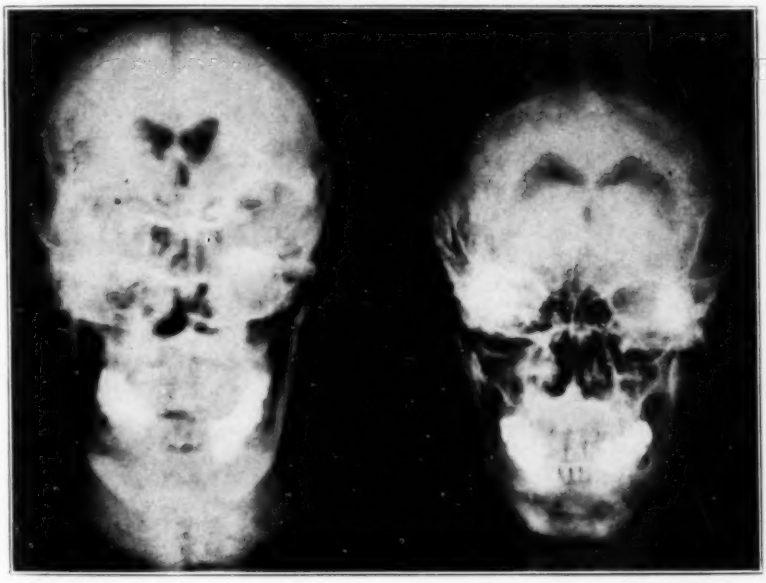

Fig. 9 (case 11).—Encephalogram (six months later), revealing the presence of a moderate asymmetric internal hydrocephalus.

and 84 diastolic. The ears and the vestibular reactions were normal. The spinal fluid was entirely normal. The Wassermann reaction of the blood was negative.

Clinical Diagnosis.—The examiners had the impression that the patient's symptoms were not organic and that the symptom complex was a mixture of hysteria and malingering.

Encephalography.—This procedure was carried out on Feb. 24, 1931, 95 cc. of air being injected. The encephalogram revealed a normal ventricular system.

Comment.—This case is instructive, owing to the fact that the clinical diagnosis of a functional syndrome was borne out by the encephalographic study.

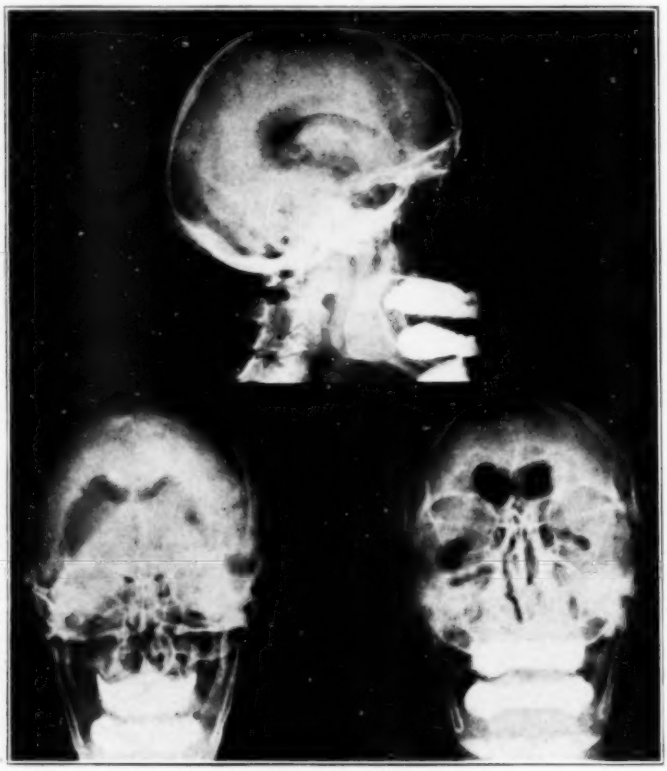

Fig. 10 (case 13).—Encephalogram, revealing a moderate internal hydrocephalus, more pronounced on the right. The absence of surface markings is to be noted (this was due to an adhesive arachnoiditis).

Case 13.—Gustav P., aged 43, a police officer, was admitted to Bellevue Hospital on Feb. 24, 1931, complaining of convulsions for ten years, and headaches for four years prior to admission. The family history was without significance. The patient had undergone a mastoidectomy in 1915, and a radical mastoidectomy at the Post-Graduate Hospital in December, 1921; a left nephrotomy had also been performed for the removal of a renal calculus in March, 1928. On Jan. 14, 1919, the patient was struck by an automobile and sustained a severe injury of the head and fractures of the left leg and right knee; he was taken to the Knickerbocker

Hospital. He bled from the nose, ears and mouth and was unconscious for ten days. In June and July, 1919, he was under observation at the Rockefeller Hospital. During this time (about six months after the injury), he had a number of generalized convulsions, which were followed by a period of confusion. In February, 1920, during one of the convulsive episodes he fractured his nose, and in December, 1928, he sustained a fracture of the right lower jaw.

Physical Examination.—There was a systolic murmur at the apex of the heart; the blood pressure was 156 systolic and 100 diastolic. There were a deformity of the lower third of the left leg (old fracture), and a healed mastoid wound. The neural status was normal, except for an equivocal plantar response on the left and a diminished left ankle jerk. There were suggestive hyperpituitary features. The spinal fluid was clear and colorless; the pressure was 160 mm.; the fluid was otherwise normal. The Wassermann reaction of the blood was negative.

Clinical Diagnosis.—The diagnosis was posttraumatic epilepsy.

Encephalography.—This procedure was carried out on March 6, 1931, 105 cc. of air being injected. The encephalogram revealed a considerable degree of internal hydrocephalus, which was more pronounced on the right. No cortical markings were seen. The observations were suggestive of adhesive arachnoiditis.

Operation and Course.—Exploration was carried out through a large temporoparietal flap. Old adhesions between the dura and the vessels of the cortex were found and freed; a small decompression in the temporal area was made. The patient's condition improved; the headaches disappeared, and the attacks became less frequent. The pathologist's report on the tissue removed at the operation was: fibrous scar tissue.

Case 14.—Sidney R., aged 26, a radio mechanic, was admitted to Bellevue Hospital on May 7, 1928, complaining of fainting spells and changes in personality. The family history was without significance. On May 6, 1922, the patient was thrown from an automobile for a distance of 45 feet; he was taken to Lincoln Hospital where he remained for seven weeks. He was unconscious for twelve hours. There was bleeding from the ears, nose and mouth. The spinal fluid was uniformly bloody on two separate occasions. Roentgen examination showed a fissured fracture in the right temporoparietal region. The patient was discharged on May 24, 1922, with a diagnosis of fracture of the skull and intracranial injury. There was a residual paralysis of the right side of the face. A number of months afterward, the patient developed personality changes, irritability and inability to carry on.

On March 20, 1928, he was seized with dizziness, fell to the ground and lost consciousness for a number of hours. On April 15, 1928, he had another dizzy spell. Neither he nor the members of his family recalled any attacks of convulsions or incontinence of urine.

Physical Examination.—There were ptosis of the right upper lid, paralysis of the right side of the face (peripheral type) and impairment of hearing on the right. Blood pressure readings were normal. Vestibular tests revealed no abnormalities aside from failure to past point with the left hand. The Wassermann reaction of the spinal fluid and blood was negative.

Clinical Diagnosis.—The diagnosis was fracture of the skull (old); posttraumatic state with epileptic equivalents.

Encephalography.—This procedure was carried out on May 14, 1928, 110 cc. of air being injected. The encephalogram revealed symmetrical dilatation of the lateral ventricles, moderate dilatation of the third ventricle and increased aeration of the subarachnoid space.

Case 15.—John S., aged 24, a mechanic, was admitted to Bellevue Hospital on March 6, 1928, with the complaint of mental confusion, loss of memory, "inability to walk straight" and loss of balance. The family and previous histories were without significance. On April 9, 1926, while riding a bicycle, the patient came into collision with an automobile. He remembered nothing until two weeks later. He sustained fractures of the skull, of the left lower jaw and of the shoulder girdle, a compound fracture of the left index finger, injury to the right brachial plexus and other minor injuries. He was in the Memorial Hospital, Rahway, N. J., from April 9 to May

Fig. 11 (case 14).—Encephalogram, anteroposterior view, revealing the presence of a low grade internal hydrocephalus with some dilatation of the third ventricle.

25, 1926. Left-sided deafness followed the injury. He was subsequently under treatment by a local physician. At various intervals since then, he had been seen as an outpatient at Bellevue Hospital. His symptoms were chiefly those already noted.

Physical Examination.—General medical examination revealed no abnormalities. Neural examination showed some impairment of the sense of smell; slight right external rectus weakness, with nystagmoid jerks in the horizontal plane, especially to the right; left-sided deafness of neural type; less active abdominal reflexes on the right, and an equivocal right plantar response. There were also signs of a plexus lesion involving the left upper extremity. There were no sensory changes, aphasia or hemianopia. The patient exhibited emotional instability, catatonic symptoms and confusion. The spinal fluid was entirely normal.

Clinical Diagnosis.—The diagnosis was fracture of the skull with sequelae.

Encephalography.—This procedure was carried out on May 21, 1928, 120 cc. of air being injected. The encephalogram revealed dilatation of both lateral ventricles, which was more marked on the right. There were also some distention of the third ventricle and moderate aeration of the subarachnoid space.

CASE 16.—John L., aged 30, a chemist, was first admitted to Bellevue Hospital on March 30, 1927. The family and previous histories were without significance. On March 30, 1927, the patient was struck on the head. He was brought to the hospital in coma and remained semistuporous for forty-eight hours. There was no bleeding from the nose, ears or mouth. Soon after admission, it was discovered that he presented a left hemiplegia, with hyperactive deep reflexes and a Babinski sign.

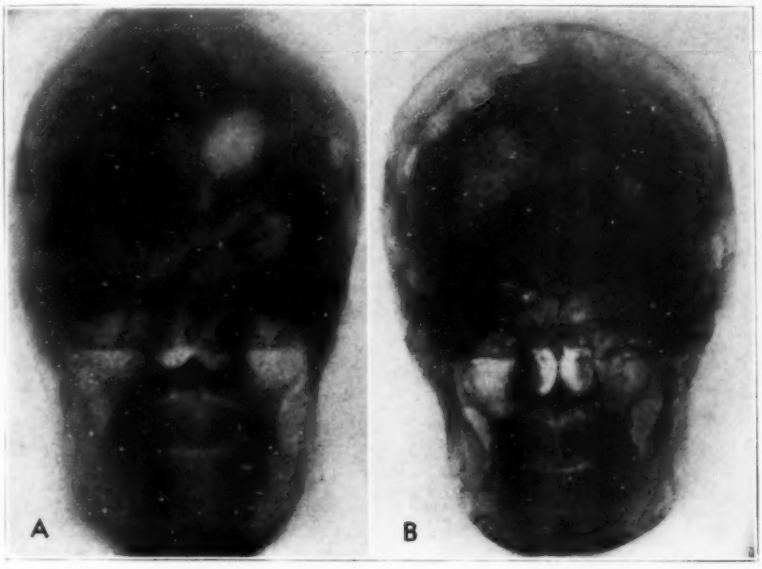

Fig. 12 (case 16).—*A*, encephalogram, anteroposterior view, revealing an asymmetric internal hydrocephalus, more pronounced on the side of the lesion, with migration of the ventricle toward the site of the postoperative scar. *B*, posteroanterior view, revealing similar findings.

He was irrational, confused and disoriented for several days. The spinal fluid was clear; the pressure was increased. Roentgen examination of the skull gave negative results.

Owing to the presence of focal signs, an operation was performed. The dura was incised and the subdural space explored. No evidence of hematoma was found. The patient was discharged from the hospital on May 5 with left-sided hemiparesis and sensory disturbances on the left (probably due to cerebral laceration or intracerebral hemorrhage).

He was readmitted to the hospital on Aug. 19, 1929. During the interval between the original injury and readmission to Bellevue Hospital, power had returned to some extent in the left lower extremity, but the upper extremity was

Summary of Sixteen Cases Reported in this Article and of Four Previously Reported

Case	Previous History	Date of Injury	Type of Trauma	Coma, Duration	Vomiting	Bleeding	Roentgen Observations	Spinal Fluid	Subsequent History	Neural Findings	Encephalography, Date and Findings
1	Neg.	Oct. 3, 1928	Blow on head by falling wall	Unconscious several hours	No	Ears; nose	Neg.	Clear; pressure, 182 mm.	Attacks of rigidity with loss of consciousness; vertigo; tinnitus in right ear	Diminished hearing on right; caloric test normal; spinal fluid normal; pressure, 160 mm.; diagnosis: posttraumatic epilepsy	Nov. 26, 1929; 110 cc. of air; internal and external hydrocephalus
2	Neg.	June, 1929	Automobile accident (overturned car)	?	?	?	Fracture of left occipital bone and of clavicle	Not done	Memory defects; epileptiform seizures; personality changes	Slight right lower facial weakness; diagnosis: posttraumatic epilepsy	Nov. 5, 1929; 110 cc. of air; increased air over brain; ventricular system normal
3	Neg.	Dec. 19, 1929	Struck on head by piece of falling iron	No	No	No	Not done	?	Loss of hearing on the right; dizziness	Left hearing normal; right, eighth nerve deafness; diagnosis: old fracture of the right petrous bone; postconcussion	Feb. 26, 1930; 90 cc. of air; internal and external hydrocephalus
4	Neg.	1920	Fall, striking head	Unconscious several hours	?	No	Positive; fracture of left occipital bone; operatoin at Fordham Hospital at once	?	Jacksonian seizures on right, 5 years later	Right-sided signs; diagnosis: posttraumatic epilepsy	March 12, 1930; 145 cc. of air; internal hydrocephalus; greater on left than on right; ventricular migration
5	Pleuropneumonia (thickened pleura)	Dec. 9, 1930	Thrown by automobile, head striking curb	Unconscious 24 hours	? Fed by tube one week	?	Neg.	Neg.	Mental symptoms; disorientation; excitement; "silly talk"	Left-sided signs; diagnosis: intracranial lesion of right hemisphere	Jan. 12, 1931; 100 cc. of air; internal and intracranial and external hydrocephalus (mild)
6	Neg.	July, 1928	Railroad accident	Unconscious 3 hours	?	Both ears	Not done; diagnosis: fracture of base of skull	Not done	Bilateral diminished hearing; greater on right than on left	Slight bilateral eighth nerve deafness; greater on right than on left; active knee jerks; diagnosis: fracture of base of skull	July 21, 1930; 100 cc. of air; moderate internal and external hydrocephalus
7	Neg.	Nov. 13, 1929	Struck on head by crowbar	Unconscious few minutes	Three or four times	No	Not done	Neg.	Dizziness; trembling; weakness; faintness	Right lower facial weakness; absent abdominal reflexes; active deep reflexes; vestibular tests normal; diagnosis: posteoncussion state	Aug. 2, 1930; 105 cc. of air; mild internal hydrocephalus
8	Neg.	Dec. 24, 1929	Struck on head	?	?	?	?	?	In hospital 2 mos.; developed convulsions (focal); weakness of right arm; diagnosis: depressed fracture; posttraumatic cortical cyst; syphilis	Right-sided signs; absent abdominal reflexes; Wassermann reaction of blood, 4+; evidence of old fracture of parietal bone on left	Dec. 18, 1930; 90 cc. of air; dilated left ventricle; increased air over brain; ventricular migration
9	Neg.	1919	Struck on right side of head	?	?	?	Depressed fracture; operation at Boston City Hospital at once	?	Weakness of left side, especially arm; convulsions on left side	Left-sided signs; motor and sensory paralysis; diagnosis: traumatic epilepsy; meningocerebral scar	Oct. 15, 1930; 90 cc. of air; internal hydrocephalus; greater on right than on left; ventricular migration
10	Neg.	1926	Thrown	Uncon-	?	?	Positive;	?	Petit and grand mal seizures 2 years later	Right hyperreflexia; Babinski sign on right; diag-	May 20, 1930; 90 cc. of air; internal and external hydro-

				Hospital at once						meningocerebral scar	ventricular migration
10	Neg.	1926	Thrown from motorcycle	Unconscious several days	?	?	Positive; operation at St. John's Hospital	?	Petit and grand mal seizures 2 years later	Right hyperreflexia; Babinski sign on right; diagnosis; posttraumatic epilepsy	May 20, 1930; 90 cc. of air; internal and external hydrocephalus; greater on left than on right
11 (Two admissions)	Neg.	Feb. 18, 1930	Struck by automobile	Unconscious several hours	Yes; headache; bradycardia; pulse 52	No	Neg.	Bloody and xanthochromic	Diagnosis (Feb.): fracture of skull, brain laceration and subarachnoid bleeding; diagnosis (June): posttraumatic headache	Abdominal reflexes diminished; increased deep reflexes	Feb. 26, 1930; 80 cc. of air; normal; June 17, 1930; 90 cc. of air; internal hydrocephalus
12	Neg.	Nov. 29, 1927	Struck on head by piece of iron	Unconscious 30 minutes	No	No	Neg.	Not done	Headache; dizziness; throbbing left ear; visual disturbance of left eye	Negative; ear tests negative; diagnosis: hysteria and malingering	Feb. 24, 1931; 95 cc. of air; normal
13	1915, mastoidectomy; 1928, nephrotomy	Jan. 14, 1919	Struck by automobile	Unconscious 10 days	?	Nose; ears; mouth	Neg.	?	General convulsions 6 months after injury to admission; headache	Left plantar equivocal diagnosis: posttraumatic epilepsy	March 6, 1931; 105 cc. of air; internal hydrocephalus, greater on right than on left; no air over cortex; (operation showed adhesive arachnoid)
14	Neg.	May 6, 1922	Thrown from automobile; hurled 45 feet	Unconscious 12 hours	?	Ears; nose; mouth	Fracture of base; seventh nerve palsy; fracture of vault also	Bloody	Fainting spells; personality changes; dizziness; irritability; no convulsions	Right seventh nerve paralysis; diminished hearing on right; diagnosis: old skull fracture; posttraumatic epileptic equivalents	May 14, 1928; 110 cc. of air; internal and mild external hydrocephalus
15	Neg.	April 9, 1926	Struck by automobile	Unconscious 2 weeks	Yes	No	Positive; fracture of skull, jaw and shoulder; injured right brachial plexus	?	Left deafness; memory defect; confusion; vertigo	Right external rectus weakness; left eighth nerve deafness; mild right-sided signs; right brachial plexus lesion	May 21, 1928; 120 cc. of air; internal and external hydrocephalus
16	Neg.	March 30, 1927	Struck on head	Unconscious; stupor; 48 hours	No	No	Neg. (operation at Bellevue Hospital at once; negative)	Neg.; left hemiplegia	Left-sided signs; motor and sensory paralysis; on left, forced grasping; left-sided twitchings; general convulsions	Left hemiparesis; left motor and sensory signs; astereognosis; diagnosis posttraumatic cerebral scar	Aug. 27, 1929; 80 cc. of air; internal hydrocephalus; greater on the right than on the left; ventricular migration
							Previously Reported				
17	Neg.	November, 1925	Struck on head by falling wall	Unconscious 3 hours	?	?	?	?	Headache and dizziness following adjudication	Negative	Oct. 23, 1928; 80 cc. of air; bilateral internal hydrocephalus
18	Neg.	1925	Automobile accident	Unconscious 20 minutes	Yes; for three or four days	No	Not done	Not done	Backache; difficulty in walking; dizziness; periodic vomiting	Increased deep reflexes; diagnosis: functional paraplegia	Aug. 9, 1928; 120 cc. of air; external hydrocephalus
19	Neg.	July, 1928	Struck on head by scaffold	Unconscious 3 hours	No	No	Not done	Not done	Headache; episodic stupor; vomiting; dizziness; no convulsions	Right diminished abdominal reflexes; diagnosis: posttraumatic psychosis	Sept. 7, 1928; 100 cc. of air; internal and external hydrocephalus
20	Fistula in ano, recurring	January, 1926	Fell, striking head	Unconscious 30 minutes	No	No	Not done	Not done	General weakness; headache; vertigo	Pupils reacted better on left than on right; abdominal reflexes diminished, deep reflexes increased; vestibular tests showed increased irritability; diagnosis: postconcussion state	June 10, 1927; 100 cc. of air; internal and external hydrocephalus

still paretic. At times the patient presented twitchings of the left upper extremity; he also had two generalized convulsions associated with loss of consciousness, one in January, 1928, and another in September, 1928.

Physical Examination.—There were left facial weakness of central type; deviation of the tongue to the left; left hemiparesis, more pronounced in the arm; a flexor contracture in the left hand with forced grasping, hyperactive deep reflexes on the left, and a left Babinski sign. There was impairment of all forms of sensation in the left upper extremity, with astereognosis in the left hand. The gait was typically hemiplegic. The spinal fluid was entirely normal; the pressure was 76 mm. The Wassermann reaction of the blood was negative.

Clinical Diagnosis.—The diagnosis was posttraumatic cerebral scar.

Encephalography.—This procedure was carried out on Aug. 27, 1929, 80 cc. of air being injected. The encephalogram revealed dilatation of the ventricles, which was more pronounced on the right, with migration of the ventricular system toward the site of the lesion.

SUMMARY

In the group of cases reported, eight presented definite evidence of fracture of the skull; in two it was suggestive; two of the cases exhibited subarachnoid bleeding following the initial trauma, but in the majority there was no evidence of either fracture ow the skull or subarachnoid bleeding. There were nine cases of posttraumatic epilepsy; six showed objective signs of a residual focal lesion in the brain. In case 16, there was evidence of a gross lesion in the substance of the brain without subarachnoid bleeding or fracture of the skull. I have recently had occasion to observe a similar instance of intracerebral bleeding following a skull injury. At autopsy, a large intracerebral hemorrhage was found without signs of disease of the cerebral vessels. There was also no evidence of fracture or subarachnoid hemorrhage.

In all but one of the cases studied, definite changes in the encephalogram were demonstrable. These consisted of dilatation of the ventricles, considerable accumulations of air on the convexity of the brain and migration of the ventricular system toward the site of the lesion. These deviations from the normal were found either separately or in combination.

It is, of course, understood that no sweeping conclusions can be drawn from this relatively small group of cases. Yet the encephalographic observations were so uniformly abnormal that they are suggestive of an organic basis for some of the symptoms in the posttraumatic state.[9] In a number of the cases signs of focal disease were demonstrated, but even in those with only general symptoms a similar process probably forms the basis of the complaints.

9. By the term posttraumatic state I mean the symptom complex following a skull injury which is accompanied by a period of unconsciousness and in which there may or may not be evidence of fracture of the skull or subarachnoid bleeding.

I believe that in cases of skull injury there may be all grades of hemorrhage, from punctate size up to gross, macroscopically demonstrable extravasations. The pathologic studies of Cassasa [10] and others, the work of Martland [11] on the symptom complex called "punch drunk" and the publication of Osnato and Giliberti [12] on traumatic encephalitis would seem to confirm this assumption.

One must bear in mind that the symptoms of the posttraumatic cerebral general syndrome (Foerster [1]) are more or less identical with those observed in arteriosclerotic disease of the cerebral vessels, and that the same grouping of symptoms is encountered in all parts of the world without any apparent opportunity for collusion between the injured persons. A number of years ago, I carried out vestibular tests in some of these cases; many of them presented increased irritability of the labyrinths with pronounced reactions to caloric tests, evidence of a lowered threshold for all stimuli.

It is important also to remember that the encephalographic observations in cases of skull injury are not essentially different from those in degenerative disease of the brain, and in cases of so-called idiopathic epilepsy which have existed for some time and which are now believed to be of angiospastic origin. It is quite likely that the pathologic changes described by Cassasa, Martland, Hortega, Penfield, Wortis, Stevenson and others, the mechanism suggested by Ricker (stasis, prestasis and local vasomotor palsy), the vasopathies and meningopathies postulated by Foerster, and the ischemic necrobioses of Spielmeyer are concerned in the production of the changes in the brain that lead to the alterations of the encephalogram in cases of skull injury.

Finally, I shall add a few remarks with regard to the normal encephalogram. No one who has had an opportunity to section a brain will fail to recall that the upper outer poles of the anterior horns of the lateral ventricles are sharply pointed. Even in cases of brain tumor one notes the tenacity with which the ventricle on the side ipsolateral to the tumor retains this sharply pointed configuration. I have been able repeatedly to convince myself of this.

It is my belief that the first expression of internal hydrocephalus consists of a blunting and rounding out of the upper outer pole of the lateral ventricle; this is the first objective evidence of hydrocephalus, whether it be of obstructive origin (in the case of neoplasm) or the result of scar formation with retraction of the tissue (in cases of degenerative disease).

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10. Cassasa, C. B.: Proc. New York Path. Soc. **24**:101, 1924.

11. Martland, H. S.: Punch Drunk, J. A. M. A. **91**:1103 (Oct. 13) 1928.

12. Osnato, M., and Giliberti, V.: Postconcussion Neurosis—Traumatic Encephalitis, Arch. Neurol. & Psychiat. **18**:181 (Aug.) 1927.

CONCLUSION

As a result of our studies, my colleagues and I have been led to revise our conception of the so-called traumatic neuroses following serious injury to the skull. On the basis of accumulating experience, we may say that, at least in some of the cases of "traumatic neurosis," definite organic changes that can be visualized in the encephalogram have been brought to light. In this field of medicine, in which diagnosis is frequently difficult, it becomes the duty of the clinician to employ every means at his command in order to arrive at a correct interpretation of the patient's symptom complex. Encephalography offers a valuable means of differentiating between organic and functional syndromes.

HEAD INJURIES: EFFECTS AND THEIR APPRAISAL

IV. EVALUATION OF EVIDENCE *

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It is manifest from the foregoing papers of this series that brain scar produces brain deformity. This deformity can now be demonstrated clinically by aerograms. It is important to consider whether such deformity must necessarily occasion abnormal function. At first sight this conclusion would be proper and right. Caution, however, must be observed, for many perversions of structure in other forms of disease such as neoplasm occur without sign or symptom. Further, complete symmetry of the ventricles cannot be postulated as constant before injury; one of my patients had an asymmetric system caused by old caisson disease. Congenital malposition and any of the exanthems with cerebral complications or vascular accident may give rise to scar formation and cavity changes.

Furthermore, a variety of technic in taking ventriculograms certainly produces a variety of pictures. An abnormal ventriculogram can be produced from a normal person if the head is ever so slightly off center in relation to the stream of penetrating rays. This consideration will impose a technic for ventriculography of constant character as a substitute for the present imperfectly standardized procedures. Therefore, in cases of head injury one must employ a uniform technical procedure, having first excluded preexisting brain injury from disease or trauma.

Then, having discovered a ventricular distortion, one must consider whether that distortion is adequate structural evidence for symptoms, often of a subjective vague and generalized character. As has just been said, cerebral distortion can occur without symptoms in other diseases; one cannot always make absolute conclusions on the basis of even so apparently dogmatic appearances as are now afforded by the x-rays; if one surrenders, in all cases, one's clinical judgment to a mechanical procedure and fails to consider the back and foreground and annectant circumstances of each case, one will make errors and fail lamentably to guard the lamp of clinical inheritance.

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* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May, 1931.

Rio Hortega, Foerster and Penfield agree that brain laceration with retention of the products of injury must precede brain scarring; Wortis has given an account of the considerable injury precedent to ventricular deformity in animals. It is incumbent on one, therefore, to satisfy one's wisdom in each instance regarding the adequacy of injury, the immediate manifestations and the validity of those of later origin.

An effort to appraise these data, proportioning knowledge concerning them, will be submitted later in the article.

Blood in the subarachnoid system was shown by Bagley to be a cause of hydrocephalus in young dogs, and Crothers' demonstration of the frequency of hemorrhagic cerebrospinal fluid in the new-born has led me elsewhere to consider the effect of such hemorrhage in increased tendency to convulsions.

The incidence of convulsions following gunshot wounds of the brain is most variously quoted. Collier, in 1924, found that from 5 to 8 per cent of such patients developed epilepsy, whereas Steinthal and Nagel's percentage was 29; on the other hand, of 603 cases of skull fracture reported by Reichmann, only 3.8 per cent showed subsequent convulsions. Such a variety of clinical statistics must come from regarding as alike many unlike abnormal conditions.

It would seem probable, after considering the histopathologic work of Foerster and Penfield, the experimental work of Bagley, Wortis and Dandy and the varied results of gunshot brain wounds and skull fractures, that a minimal premise for immediate or subsequent convulsions is either laceration and scarring of the brain or blood in the subarachnoid space.

The origin of the fit so produced varies with the part of the brain affected; petit mal is almost certainly a change in consciousness from frontal disorder and, emerging from injury, is curiously rare; complex visual auditory and psychic hallucinations, from disorder in the temporosphenoidal lobes, and gross color fits, from disorder in the occipital poles; the great fit is an involvement of the entire cortex. The narcolepsies and cataplexies have not come under my observation as a result of head injury. On the other hand, psychic equivalents are not uncommon; one of our Bellevue patients had episodes of complete amnesia lasting twenty minutes and more, and another's emotional tempests vanished after the removal of a piece of bone that compressed the left frontal lobe. Such sequelae of skull injury with frank cerebral involvement are easy to appraise; it is different in cases with subjective symptoms only; these have been called in this country "postconcussion syndromes," an unsatisfactory variant on Foerster's "posttraumatic general cerebral syndrome." The usual complaints are headache, rarely localized, and dizziness, especially on stooping; these

symptoms often are made worse by "bad weather" and "constipation," they can often be controlled or ameliorated by small amounts of sedatives, and not infrequently the patient states his inability to work.

If the original injury and immediate manifestations of injury were severe and residual symptoms persist, with ventricular distortion to boot, it is fair to assume that localized meningitic change has occurred, giving rise to cerebromeningeal adhesions, as a competent producing cause for the symptoms. However, there is no authority to hypothecate cerebromeningeal adhesions if the roentgenograms and spinal fluid were normal at the time of injury, and the ventricles later are found undisturbed. Of course, scalp or skull sepsis complicating the trauma might produce local meningitic involvement that otherwise would not occur.

Nevertheless, it must be stated that a very small minority of patients with head injuries, including those with skull fracture, return to the hospital later with any complaint whatever; probably many of these people have misshapen ventricles without symptoms or with such as do not seem to them to require aid. Indeed, distorted ventricles exist as a result of many different conditions without giving rise to any subjective unpleasantness; porencephalic children will come at once to mind, and long-standing cerebral vascular accidents in young or middle-aged people rarely give rise to any signs or symptoms other than those that result from local brain injury. Therefore, one is in no position to argue that distorted ventricles are necessarily associated with symptoms, and the corollary follows that a distorted ventricle is not always associated with cerebromeningeal adhesions, nor indeed do all such adhesions produce distorted ventricles.

There is yet another factor to be reviewed before one can feel that even-handed justice has been given this matter; the mental and emotional condition of the person who has been struck near, as it were, where he lives! Suggestion plays a major part in mental life; one readily adopts an idea in agreement with an already established emotional trend. One might liken agreeable suggestion to the hitting of a ball in the way it is going, and adverse criticism, in the way it is coming.

Fear in an injured man can always be played on by a gloomy medical prognosis, an acquisitive legal opinion or a solicitous and avaricious relative. The procession of workmen who have met with minor injuries to the head and remain often for years incapable of daily effort compares strangely with the polo players and the footballers of our acquaintance who so often need forcible restraint to interrupt their sporting careers. Nor do such workmen usually consciously affect their symptoms; their system of false suggested ideas is built of funk

and subliminal desire. To buttress their invalidism by sonorously vague diagnoses is in many instances to segregate a good workman from his happiness.

One must seek harmony between the degree of injury, the subsequent history of the patient's symptoms and his physical condition; dissonance in this trilogy must be viewed askant and awake a suspicion of a suggested neurosis.

A practical solution of these problems is needed; failing such, neurologists are but as the philosophers of Laputa, distilling sunshine out of cucumbers.

To estimate the organic disability in a particular case, the following plan is therefore tentatively offered: What are the criteria of head injury sufficient to produce organic change in the brain? These criteria are:

A. Absolute criteria:

(1) Roentgen evidence—skull fracture
(2) Bloody spinal fluid
(3) Bleeding from the orifices—especially from the ears
(4) Focal cerebral palsies

B. Presumptive criteria in the order of their importance:

(5) Convulsive states, proved to be posttraumatic
(6) Ventricular distortion, proved to be posttraumatic
(7) History of prolonged unconsciousness
(8) History of adequate trauma, with especial consideration of the occurrence of vomiting following the injury.

These units are in a real sense measurable and are instruments for establishing the fact of brain injury. The first four units together with 7 and 8 can be determined with accuracy. Convulsive states are often complained of but are not always readily seen. One may satisfy oneself of their reality by provoking an attack in many instances by cocaine or hyperventilation; this evidence is of value when positive.

Headache and dizziness are well nigh imponderable factors after head injury. However, if they persist for more than four months in a man under 60, ununited to any of the first seven premises of brain injury, they are to be regarded as suggested neuroses unfounded in structural change.

ABSTRACT OF DISCUSSION

Dr. Wilder Penfield, Montreal: There are many points of great interest in these communications. In regard to the headache and dizziness that follow such injuries, I think we should bear in mind the type of headache and the type of dizziness, as indicated by the patient's description, in distinguishing the real from the unreal. A patient with a true posttraumatic headache describes his headache as being always in the same place.

It usually has a time in the day when it is worse. It must also be accompanied by dizziness if one is to be sure that one is dealing with that type of headache, and the dizziness itself is of a certain characteristic type. It lasts for from a minute to ten minutes; it comes on at any time. If the patient is walking at the time of the dizzy spell, he has to stop and wait. He sometimes describes it as a darkness and not a dizziness. Sometimes it seems to him to be visual. This type of meningeal headache and dizziness can in a certain percentage of cases be completely abolished by the spinal insufflation of air.

I would like to ask a question in regard to the epileptic patient who was treated surgically, the patient who had dilated ventricles and no air in the subarachnoid space. He represents an extremely interesting group; I have seen a few, and I should like to inquire how the block was cleared up. As the air passed from the spinal canal into the ventricles freely, the block could not have been in the roof of the fourth ventricle, and I should like to know how to clear up such a block, which must lie at the base or on the surface of the brain.

Our experience agrees altogether with the technic of taking encephalograms that has evidently been used. In our experience encephalograms made in the erect position give much less accurate information and much less helpful guidance than those taken with the patient in the horizontal position. In the erect position the ventricles must be completely filled in order to see small deviations of the third ventricle and the body of the ventricle. Our belief is that the most helpful type of plate in these cases is one taken with the patient lying on his back with his brow up, and we make it a practice to take two plates in that position, one at the beginning and one at the end. One is developed more completely than the other, so that one shows the anterior horns that are spread out wide, and the other the body that shows the typical butterfly shape.

We have also been quite impressed by the fact that the use of oxygen rather than air gives rise to very much less postinjection headache and to the disappearance of the gas at a much earlier date after its injection.

Dr. S. Bernard Wortis, New York: I cannot tell Dr. Penfield what was done surgically, not having been present at the operation.

Dr. Foster Kennedy, New York: We are more than willing to accept Dr. Penfield's admirable suggestion as regards the type of headache and as regards the dizziness. Of course, in cases fulfilling those requirements, the patients ought to be treated by spinal insufflation, encephalograms being taken; in fact, they would probably be cured thereby if the cases were of organic character, and we would obtain the information my paper was designed to show we need to distinguish the neuroses from the organic cases. I think that Dr. Penfield has given us an admirable answer in regard to my demand for a standardized technic in encephalography.

THE DIFFERENTIAL DIAGNOSIS OF TUMOR OF THE BRAIN

THE IMPORTANCE OF CONSIDERING RENAL HYPERTENSION WITH CHOKED DISK *

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The diagnosis of tumor of the brain is rarely an easy problem. Apart from the neurologic symptoms, which unfortunately may be at times strikingly indefinite, the presence of headache, vomiting and choked disk go far to suggest the presence of an intracranial mass lesion. Of this triad, choked disk is unquestionably the finding that most strongly indicates the presence of a tumor of the brain.

However, in the past two years, five cases have been encountered in the neurosurgical clinic of the University Hospital referred as cases in which tumor of the brain was suspected on the basis of a choked disk, headache and suggestive neurologic signs. Subsequently, a more thorough investigation seemed to prove definitely that vasculorenal disease was the cause of the symptoms. Nevertheless, before this fact was convincingly demonstrated, the neurologic symptoms and evidence of intracranial pressure appeared positive enough in two instances to warrant an exploration for tumor of the brain.

The combination of arterial hypertension and retinal changes has long been associated with renal disease. But what may not be so widely appreciated is the fact that hypertension may be present and the retina show a papilledema at times indistinguishable from that due to intracranial pressure before studies of the urine show more than a suggestion of renal disease or analysis of the blood any evidence of nitrogen retention. It is in this particular group of cases, especially if striking neurologic symptoms are present, that an erroneous diagnosis of tumor of the brain may easily be reached.

The term "malignant hypertension" has been used by Volhard and Fahr [1] to describe vascular sclerosis in certain cases in which there later

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* From the Neurosurgical Clinic of the University Hospital.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

1. Volhard and Fahr: Die brightsche Nierenkrankheit, Klinik, Pathologie und Atlas, Berlin, Julius Springer, 1914, p. 247.

develops definite renal insufficiency. Wagener and Keith [2] and Keith, Wagener and Kernohan [3] separated out a group of cases in which severe vascular disease was shown without distinct renal insufficiency and classified them as cases of "malignant hypertension." The latter authors held that "the term 'malignant' is applicable to these cases because of the frequent loss of weight, cerebral symptoms and accidents, continued high blood pressure, severe neuro-retinitis and the serious prognosis. The persistent hypertension, cardiac enlargement, peripheral sclerosis, retinal changes, absence of anemia and only moderate or no reduction in renal function seem to constitute a distinct clinical entity."

It is into the "malignant hypertension" group that the cases here described fall. That a diagnosis of tumor of the brain was reached in two instances is not without precedent. Wagener and Keith [2] suspected tumor of the brain in three of their cases, in one of which a decompression was performed. Murphy and Grill [4] reported similar difficulties in differential diagnosis. In the three patients here described on whom an operation was not performed, the lack of positive neurologic symptoms and evidence of peripheral arteriosclerosis, coupled with obvious hypertension, made the proper diagnosis apparent.

In differentiating between tumor of the brain and "malignant hypertension" accompanied by neurologic symptoms, the importance of the hypertension should never be overlooked. While it is always possible that a patient harboring a tumor of the brain may show a coincidental high blood pressure, the increased vascular tension is never due to the presence of the tumor alone. That hypertension can be accompanied by increased intracranial pressure is obvious from the cases here described, as well as from the report of Larsson,[5] in all of whose eleven patients with hypertensive neuroretinitis a spinal tap showed an elevated pressure. Fishberg and Oppenheimer [6] stressed the frequency with which headache accompanies the cerebral edema noted in this condition. Lastly, with regard to the changes seen in the eyegrounds in "malignant hypertension," Wagener [7] stated that in all his cases "hyperemia and edema of the disc were characteristic features. The edema of the discs varied from less than one diopter to six diopters, was usually an outstanding feature, and was often relatively more

2. Wagener and Keith: Cases of Marked Hypertension, Adequate Renal Function and Neuroretinitis, Arch. Int. Med. **34**:374 (Sept.) 1924.

3. Keith; Wagener, and Kernohan: The Syndrome of Malignant Hypertension, Arch. Int. Med. **41**:141 (Feb.) 1928.

4. Murphy and Grill: Arch. Int. Med. **46**:75 (July) 1930.

5. Larsson: Acta ophth. **1**:193, 1923.

6. Fishberg and Oppenheimer: Hypertensive Encephalopathy, Arch. Int. Med. **41**:264 (Feb.) 1928.

7. Wagener: Tr. Am. Ophth. Soc. **25**:349, 1927.

severe than the other retinal conditions such as edema of the retina, hemorrhages and exudates. *In some cases* (italics mine) it was differentiated from choked disc largely by the presence of sclerosis of the retinal arteries." Fishberg and Oppenheimer [8] said: "As a result of the circulatory disturbance in the retina produced by increased intracranial tension (e. g., tumors of the brain with choked disks) changes may appear in the retina indistinguishable from those of malignant hypertensive neuroretinitis. The manifestations of increased intracranial pressure, headache, nausea, vomiting, convulsions, choked disk and high pressure of the cerebrospinal fluid may so dominate the clinical picture that a diagnosis of tumor of the brain is made." All the cases here reported showed various degrees of retinal arteriosclerosis as well as choked disk. If a patient with these ophthalmologic signs is seen on the medical wards, where hypertensive conditions are more common, the examiner probably stresses the arteriosclerosis as shown by the tortuosity of the vessels and the irregularity of their caliber. But on a neurosurgical service, where tumor of the brain is suspected, the choked disk as a sign of intracranial pressure in all likelihood receives the major emphasis in the report.

The frequency with which hypertension is accompanied by symptoms indicating a lesion in the brain is widely recognized. The determination of whether the neurologic signs are due to vascular disease alone or to a coincidental mass lesion which might be relieved by surgery is the point at issue. The cerebral symptoms of themselves offer no clue unless the manner of their onset or their diffuse nature suggests vascular disease rather than tumor. While an encephalogram could rule out tumor, the report of Rosenheck,[9] indicating that the injection of air in the presence of high blood pressure may precipitate a further intracranial hemorrhage, makes this procedure seem too hazardous. Although Keith, Wagener and Kernohan and Cushing and Bordley [10] stated that following exploration and decompression, intracranial pressure was relieved and papilledema disappeared, this operation in the cases here reported failed to accomplish these results. As visual loss is not an urgent indication for decompression in these cases, it seems proper, when hypertension without renal symptoms complicates a clinical syndrome suggesting tumor of the brain, to keep the patient under close observation for an extended period. If further neurologic evidence suggesting tumor develops, surgery may seem indicated, and

8. Fishberg and Oppenheimer: Differentiation and Significance of Certain Ophthalmoscopic Pictures in Hypertensive Diseases, Arch. Int. Med. **46**:901 (Oct.) 1930.

9. Rosenheck: Encephalography: The Development of Hemiplegia Following Its Use, with Report of a Case, Arch. Neurol. & Psychiat. **22**:575 (Sept.) 1929.

10. Cushing and Bordley: Am. J. M. Sc. **136**:484, 1908.

the hypertension be held to be coincidental. In the meantime, however, evidence of renal damage may appear, which will allow a correct diagnosis to be made.

Two of the cases reported here presented nice problems in diagnosis. Both occurred in relatively young persons in whom arterial disease was unexpected. In neither were the peripheral arteries pulsating or sclerotic. In both, the evidence of renal disease was very slight. The mild hypertension in case 1 should have given a clue to the true condition. But with the sudden onset, positive neurologic signs, choked disk and intracranial pressure, the diagnosis of tumor seemed well supported. In case 2, the long history with repeated attacks of paralysis plus hypertension should have raised a grave suspicion that the cerebral lesion was not one calling for surgical treatment. In fact, a vascular lesion was suspected, and a transfer of the patient to the medical wards for further study was made. When little or no evidence of arteriosclerosis or of renal disease could be found, surgical intervention seemed justified. Although a tumor of the brain or other intracranial lesion causing increased intracranial tension never of itself elevates the blood pressure, there was no real reason to suppose that the patient might not have a tumor of the brain and coincidental hypertension.

In three cases the neurologic signs were never sufficient to warrant surgical intervention. In case 3, the possibility of a chronic subdural hemorrhage was considered, because of the history of an injury to the head. In cases 4 and 5, the manner of onset of the symptoms and the results of the physical examination made the proper diagnosis apparent.

SUMMARY

Five cases of malignant hypertension are presented. In every instance, headache, vomiting and choked disk were noted. In none of the cases at the first examination was sufficient evidence of renal disease shown to force consideration of nephritis as the underlying cause of the hypertension. Three of the patients were too young to make generalized arteriosclerosis seem probable, and only one of the three showed definite evidence of hardening of the peripheral vessels. In the two other subjects, rigidity and pulsation of the temporal, brachial and radial arteries were noted. Two of these young persons without sclerotic peripheral vessels showed such definite neurologic evidence of a cerebral lesion, coupled with papilledema and increased intracranial tension on lumbar puncture, that a diagnosis of tumor of the brain was made. Surgical exploration failed to reveal a tumor. Furthermore, the decompression left at the operation failed to reduce the papilledema, although in one case the headache was relieved.

All of the patients died within six months after discharge from the hospital, an evidence of the serious prognostic import of papilledema in hypertension.

REPORT OF CASES

CASE 1.—*History.*—A boy, aged 10, who was admitted to the University Hospital on June 19, 1930, complaining of headache and weakness of the left side of the face, had had frontal headaches for the past three years. Attacks occurred two or three times a week, with at times a period of two weeks between attacks. Usually there were nausea and vomiting with the headaches, which lasted from two to four hours. Between attacks the boy felt perfectly well. Eleven days before admission, it was noticed suddenly that he had weakness of the left facial muscles. This had come on without apparent cause, as he had not been exposed to a draught or to cold. There had been no impairment of hearing or drowsiness. The patient talked and cried a great deal while asleep and at times walked in his sleep. He had noticed no marked impairment in vision. His appetite was poor. He had lost a little weight. There were no pulmonary or cardiac symptoms. There had been some nocturia in the past two years. The past medical history showed that the patient had had mumps in childhood and a tonsillectomy in 1927. He was born by cesarean section. Prior to the onset of the present symptoms, he had been in good health. The family and social history was unessential.

Examination.—The results of physical examination were negative except that the blood pressure was 150 systolic and 70 diastolic. No sclerosis of the peripheral blood vessels was noted. Neurologically, slight ataxia and awkwardness were noted in the movements of the left hand; there was weakness of the left side of the face, of the peripheral type, together with some diminution in all the reflexes. No pathologic reflexes were noted. Ophthalmoscopic examination showed that the media were clear, and that the retinal arteries were contracted, sclerotic and tortuous, with engorgement of the retinal veins. Many flame-shaped retinal hemorrhages and an occasional ill-defined yellowish-white retinal exudate were noted. The disks were gray and hyperemic, with obliteration of the disk margins; 3 diopters of choking was recorded. The visual fields were normal. Roentgen examination of the head gave negative results. Studies of the blood showed 4,200,000 red cells and 79 per cent hemoglobin. Studies of the urine on two occasions gave essentially negative results; the specific gravity was 1.020.

Diagnosis.—Tumor of the left cerebellar hemisphere was diagnosed.

Operation.—Both ventricles were tapped and found to be distended with fluid. Suboccipital craniectomy showed a questionable enlargement of the left cerebellar hemisphere. The plunging of a brain cannula into this region failed to reveal any evidence of a cyst or a solid tumor.

Course.—Postoperative convalescence was uneventful. The patient was discharged from the hospital on July 18, 1930, and was seen in the follow-up clinic on Oct. 15, 1930, and Jan. 7, 1931. Examinations on these dates showed that there was some bulging at the site of operation, that the blood pressure was still 160 systolic and 90 diastolic, and that there was 2 or 3 diopters of choked disk, with tortuous sclerotic retinal vessels, many hemorrhages and a large exudate. The persistence of the hypertension and the fact that the retinoscopic picture had not changed, although a decompression had been made, led me to the suspicion that renal disease was the correct diagnosis. The patient was therefore readmitted to the hospital on Jan. 21, 1931, six months after the previous discharge.

The patient had been much improved until December, 1930; then the right eye became bloodshot, glassy and staring. Excessive lacrimation was noted in this eye. Vision had become somewhat impaired. There had been entire freedom from headaches since the operation. Marked emotional instability with frequent fits of anger had appeared. Occipital pain occurred when pressure was applied to the decompression at the back of the head. The boy tired easily and became drowsy. Early in January, he had an attack of vomiting. He had had occasional attacks of pain in the epigastrium. The appetite was good; there had been no loss of weight. No precordial pain, palpitation or edema had been noted. He had kept up with playmates in all games. Aside from an increasing nocturia, he had had no urinary symptoms.

Examination on Readmission.—The boy was alert and intelligent. The suboccipital flap was slightly tense, but not bulging. The cranial nerves were entirely normal. The chest was normal. The heart showed a moderate enlargement to the left; the apical beat was seen and felt in the fifth interspace, 10 cm. to the left of the midline; the second sound at the base was accentuated; the rate and rhythm were normal. In the abdomen, the lower edge of the liver was distinctly palpable below the costal margin. The extremities were normal, except for marked pulsation and some hardening in the radial and brachial arteries of each arm.

Neurologic examination gave negative results, all the cerebellar symptoms having disappeared.

The blood pressure was 256 systolic and 220 diastolic. Laboratory examinations showed a definite trace of albumin, a few hyaline casts and occasionally a granular cast in the urine. The concentrating power was good, the specific gravity varying from 1.015 to 1.027. The blood urea nitrogen was 12 mg. per hundred cubic centimeters. Lumbar puncture revealed a pressure of 230 mm. of water. An electrocardiogram showed a simple tachycardia with marked left axis deviation. An orthodiagram of the heart showed it to be somewhat displaced to the left, with moderate hypertrophy of the left ventricle. The aorta was moderately dilated and increased in density. The left ventricle and the aorta showed increased pulsatory excursion.

Retinoscopic examination showed clear media, 6 diopters of choking in each eye and many fresh hemorrhages and snow bank exudates over the retina. The arteries were markedly sclerosed, and indented the veins wherever they crossed them. The disks appeared whiter and less hyperemic than at the previous admission. The visual fields were normal.

Diagnosis.—The diagnosis was changed from suspected tumor of the brain to malignant hypertension and nephritis.

Course.—During the stay in the hospital, with rest in bed, limitation of fluids and a diet low in protein, the blood pressure was reduced to 200 systolic and 160 diastolic. The patient was discharged with the conditions improved on Feb. 11, 1931. He died in coma three months later. His physician stated that the suboccipital decompression was never distended. It was his opinion that the patient died from nephritis. However, an autopsy was not obtained.

CASE 2.—*History.*—A white woman, aged 22, married, who was admitted to the neurosurgical service of the University Hospital on Nov. 26, 1928, with the complaint of weakness of the entire right side of the body, had complained, nine months before, of being easily fatigued and of frequent frontal headaches. Vomiting attacks occurred, which were nonprojectile. Three weeks later, she had a sudden attack of unconsciousness ushered in by loss of vision. She was unconscious for two weeks. The entire right side of the body was paralyzed, and the extremities felt

numb and dead. The right side of the face and head seemed to have lost all sensation, but there was no facial paralysis. The patient was aphasic. When she recovered, she could see only directly ahead and to the left. During the next six months, she slowly recovered power in the right extremities, and speech became normal. However, she walked with a paralytic gait, there were marked sensory disturbances on the right side, and the right homonymous hemianopia remained. Severe headaches continued. Some cardiac palpitation had been noted, and also slight swelling of the right ankle and hand. No other cardiac symptoms were present. There were no pulmonary symptoms. The patient had continuous vomiting spells until four months before admission and was chronically constipated; she had had nocturia from four to six times during the past two years, but no burning or other troubles in voiding. She lost 40 pounds (18.1 Kg.) in weight in the first six months of illness, but had now gained 35 pounds (15.7 Kg.).

The menses had begun when she was 12 years old and were regular until the onset of the present illness, during which she had not menstruated. The past medical history included frequent attacks of tonsillitis and "growing pains," which may have been rheumatic. Tonsillectomy was performed on the patient when she was 14. In 1925-1926, she had had abortions performed. She was told that she had thyroid trouble, and pus and albumin in the urine. Two months after the second abortion, a left facial paralysis, both motor and sensory, developed, accompanied by a loss of the sense of taste in the left side of the tongue. She recovered from this in five weeks, only to have a right facial paralysis, both motor and sensory, appear three days later. Within five months, the face had again returned to normal. The family and social history was not important.

Examination.—The patient was cooperative and alert, with a mild right hemiparesis of the face and extremities. Speech was normal. There was a complete sensory loss on the right side. The gait was hemiplegic. Ataxia was present in the right extremities, probably owing to weakness. Astereognosis was present in the right hand from the sensory loss. The cranial nerves showed a right homonymous hemianopia, hypesthesia in the sensory zone of the right fifth and weakness of the right seventh. All reflexes on the right were exaggerated, with a Babinski sign and clonus.

The lungs and the abdomen were normal. The heart was enlarged to the left A distinct systolic thrust could be felt over the greater part of the pericardium. The cardiac rhythm was regular and the rate slow, and the sounds were of good quality. At the apex, there was a systolic murmur, which was transmitted to the axilla. The blood pressure was 195 systolic and 130 diastolic in each arm. At times during hospitalization the systolic pressure was as high as 220.

Laboratory studies showed that there was a mild degree of anemia, the red cells varying between 3,900,000 and 4,100,000, with 7,500 white blood cells. Fourteen separate urinalyses showed that the specific gravity varied between 1.008 and 1.015. A faint trace of albumin was occasionally found; on two occasions hyaline casts were reported. In twenty-four hour specimens of urine, the specific gravity varied from 1.013 to 1.015, 1,400 cc. being passed in twenty-four hours. The elimination of intravenous phenolsulphonphthalein on three occasions varied between 35 and 60 per cent. A Mosenthal concentration test showed a specific gravity varying from 1.015 to 1.020, 1,300 cc. of urine being voided in twenty-four hours. The urea nitrogen of the blood on two occasions was 16 mg. per hundred cubic centimeters. Roentgen examination of the chest showed that the heart was within normal limits of size, but that there was some widening of the arch and ascending portion of the aorta. Roentgen examination of the head gave evidence of intracranial pressure as shown by slight convolutional atrophy. The pituitary fossa

was normal. Lumbar puncture on two occasions showed a pressure of 280 and 300 mm. of water, respectively. The cell count and the Wassermann reaction of the spinal fluid were negative. The Wassermann reaction of the blood was negative.

Studies of the visual fields showed a complete right homonymous hemianopia, extending through the fixation point. Retinoscopic examination showed that in both eyes the media were clear, with contracted retinal arteries and normal retinal veins. There were a number of old, white retinal exudates about the disks, extending out to the cornea, with fairly clean-cut margins. The disks were gray and hyperemic and had fair vascularity. There was 2 diopters of choking in each eye.

Course.—The patient was referred to the medical ward, where substantially the same general observations were recorded. An electrocardiogram showed an increase in the size of the Q-R-S waves, suggesting a cardiac enlargement and a simple tachycardia, but no evidence of myocardial degeneration. The medical opinion was: Possibly the diagnosis should be cerebral hemorrhage, or a tumor or cyst of the brain. "We are confident that advanced renal disease can be excluded on the following grounds: several essentially negative urinalyses; normal blood urea nitrogen, and an only slightly reduced phenolphthalein output. The diagnosis of essential hypertension may be correct, although it is unusual at this age. Although there is not confirmatory evidence in the state of the peripheral arteries, or in the retinal vessels, it does not seem probable that the hemiparesis, the homonymous hemianopia and the edema can be explained solely by cerebral hemorrhage. It is more likely that the vascular hypertension results from the increased intracranial pressure, and that this increased pressure results from a brain tumor which is conceivably the site of subsequent intracranial hemorrhage. The neurological findings would seem to localize the neoplasm on the left side between the optic chiasm and the occipital lobe. I believe that an encephalogram is indicated and that the risk is justifiable because of the impending danger of blindness if intracranial pressure is unrelieved."

Operation.—As the patient had been referred to the medical wards to obtain an opinion as to the possibility of nephritis being the cause of the hypertension, and since it was thought that if the possibility of nephritis as a factor in the condition could be eliminated, an intracranial neoplasm was the most likely cause of the condition, a left parietal bone flap was turned down. The dura was found to be tight and tense. On reflecting the dura, one or two cortical vessels ruptured spontaneously. Bleeding was controlled only with great difficulty. Further trouble in the control of hemorrhage from the middle meningeal artery was encountered. Except for the rigidity and overdistention of the cortical vessels, nothing on the surface of the brain suggested the presence of an underlying tumor. Puncture of the brain revealed no evidence of a lesion. The condition of the arteries however, was striking. Once the dura was turned back and its support removed, it seemed as though the lightest touch would cause hemorrhage from the cortical vessels. After a painstaking hemostasis, the bone flap was replaced and the wound sutured.

Subsequent Course.—Postoperative convalescence was uneventful, except for the fact that the left cerebral symptoms increased. The patient became entirely aphasic, and the weakness of the right side was much more marked. The increased intracranial tension was controlled by lumbar puncture, which showed a pressure of over 350 mm. of water. On several occasions 50 per cent dextrose was also given by vein. Within ten days, however, the condition was much improved. The aphasia cleared up, and the hemiparesis was no more pronounced than it had been before the operation. Following discharge, symptoms of intracranial pressure increased. The headache was more severe, and herniation of the osteoplastic flap

occurred. This was controlled by repeated lumbar puncture. A report from the physician in charge stated that in the two months following discharge from the hospital the patient became practically blind, and the aphasia recurred; the blood pressure increased to 280 systolic and 220 diastolic, with a spinal fluid pressure of 40 mm. of mercury. The patient died in coma ten weeks after discharge from the hospital. An autopsy was not permitted.

CASE 3.—*History.*—J. R. W., a white man, aged 34, who was admitted to the neurosurgical service of the University Hospital on April 24, 1929, complained of persistent pain in the left parietofrontal area near the vertex. The pain had followed a severe blow in this region six months previously. At the time of the injury, the patient was not unconscious, but was somewhat bewildered and had to sit down. He suffered from a sensation of nausea, but he did not vomit and within a short time returned to work. The pain commenced that night. It had varied in intensity, at times becoming severe and radiating downward into the left supraorbital region. Twice the pain had been of sufficient severity to arouse the patient from sleep, but ordinarily he was not kept awake. Two weeks after the injury, he had a severe attack of influenza. Five weeks before admission, because of the intermittent pain, nervousness, irritability, persistent sweating and weakness he stopped work and went to the seashore for three weeks. He had two severe nosebleeds during this time, and his condition was not improved. Since the injury, he had had no vertigo, attacks of syncope, localized or generalized convulsions and except for stiffness of the right arm, no focal symptoms. In the past five months, he had shown marked loss of ambition and vigor. When he was excited cardiac palpitation and nervousness developed. No gastro-intestinal symptoms had been noted other than poor appetite. There had been no genito-urinary symptoms.

The patient's past medical history revealed measles at the age of 6, a scalp laceration that had required suturing at the point of the present pain, and five years service as sergeant-major in the English army during the war. He denied having had venereal disease. The family and social history was irrelevant.

Examination.—There were: marked generalized arteriosclerosis, a blood pressure of 160 systolic and 110 diastolic, accentuation of the second aortic heart sound and a general appearance suggesting early acromegaly. Neurologic examination gave negative results.

Laboratory studies revealed a normal blood picture, and urine with a specific gravity varying from 1.007 to 1.015 and containing a trace of albumin and hyaline casts. The urea nitrogen of the blood was 28 mg. per hundred cubic centimeters; the elimination of phenolsulphonphthalein was 55 per cent. Serologic tests of the blood and spinal fluid gave negative results. A spinal tap revealed a pressure of 320 mm. of water.

Examination of the eyegrounds showed clear media, marked thinning and tortuosity of the arteries of the retina and disks, and many flame-shaped hemorrhages and yellowish patches of exudate along the vessels. There was a choking of the disks of at least 3 diopters in each eye, with some edema of the retina. Vision was normal; the perimetric fields were full.

Diagnosis.—When the patient was first seen, a diagnosis of chronic subdural hemorrhage was entertained, in view of the localized headache, the history of injury of the head, the choked disks and the increased pressure of the spinal fluid. However, the evidence of arteriosclerosis in the peripheral vessels, the hypertension, the casts in the urine, and the evidence of nitrogen retention gave definite indication of renal disease. Further studies in the medical wards confirmed the diagnosis of arteriosclerosis and chronic glomerulonephritis. After a number of

discharges and readmissions, the patient died in the medical ward on June 6, 1930. On the day before death, laboratory studies of the blood showed 17.1 mg. of creatinine and 194 mg. of urea nitrogen per hundred cubic centimeters. Death resulted from myocardial insufficiency and the resultant pulmonary edema.

Autopsy.—The chief features observed were: generalized arteriosclerosis, myocardial hypertrophy and degeneration, and subchronic diffuse glomerulonephritis with malignant arteriolar sclerosis.

CASE 4.—*History.*—W. R., a colored boy, aged 15, was admitted to the neurosurgical service at the University Hospital on June 28, 1928, complaining of headache and vomiting, which had been noted for one month. The headaches centered in the occipital region and radiated into the left frontal area. The pain was most severe in the morning. Vomiting accompanied the headache and was at times preceded by nausea, but was frequently projectile. When the headache was most severe, the boy became dizzy and had difficulty in walking. Objects seemed always to move to the left. For the past three months, he had had an almost constant sensation of running water in the left temporal region. This noise was more pronounced when he turned the head to the right than when to the left. There had been no diminution in hearing. For the past month, he had had an occasional period of diplopia, and vision had been somewhat obscured with specks before the eyes. He had had several attacks of epistaxis. Once or twice the ankles had been slightly swollen in the morning. The appetite had been good; the bowels were constipated. There had been no gastro-intestinal or pulmonary symptoms and no genito-urinary symptoms other than occasional nocturia. There were no muscular weaknesses, sensory changes or paresthesias, and no aphasia, failing memory or convulsions. The past medical history revealed whooping cough, measles, chickenpox and mumps. There had been no tonsillitis, chorea, rheumatic fever, diphtheria or scarlet fever. The family and social history was irrelevant.

Examination.—The boy was muscular, but gave gross evidence of ill health. He was able to walk, but staggered a little, and the gait was uncertain and on a wide base. The positive findings were: changes in the contour of the incisors, suggesting Hutchinson's teeth; some enlargement of the heart to the left with accentuation of the second aortic sound; fairly pronounced sclerosis of the radial, brachial and temporal arteries for his age, and a blood pressure of 145 systolic and 110 diastolic. The chest, abdomen and extremities were normal.

Neurologic examination showed a slightly uncertain gait, a questionable Romberg sign, slight ataxia and dysmetria in the left extremities and some loss of grip in the left hand. The cranial nerves, except for the retinoscopic results, were normal. The reflexes were normal. No pathologic reflexes were noted.

Ophthalmoscopic examination showed the media to be clear, with 3 diopters of choked disk in each eye, hyperemia of the disk with marked blurring of its margins, narrow sclerotic arteries and engorged veins. The arteries indented the veins where they crossed them. A single, small, flame-shaped hemorrhage was present in the left retina. Perimetric studies showed normal fields. Vision in each eye was 6/6.

A blood count showed 4,400,000 red cells, 7,500 white cells and 75 per cent hemoglobin. Urinalyses showed a specific gravity of from 1.004 to 0.1020, with on one occasion a few hyaline casts. Urine concentration tests produced a specific gravity varying from 1.017 to 1.027. The spinal fluid pressure was 320 mm. of water; the globulin content was + 8. Serologic tests of the blood and spinal fluid gave negative results. Roentgen studies of the chest showed nothing abnormal, but those of the skull showed an enlargement of the pituitary fossa to

15 mm. anteroposteriorly, and to 12 mm. in depth, suggesting a pituitary lesion. The basal metabolic rate was —2. The urea nitrogen of the blood was 19 mg. per hundred cubic centimeters. The elimination of phenolsulphonphthalein after intramuscular injection was 60 per cent in two hours.

Diagnosis.—Opinion on the neurosurgical service varied between renal hypertension and a midline cerebellar tumor. As there was no loss of visual acuity in spite of the choked disks and increased intracranial pressure, it was decided that it would be safe to wait to see whether rest in bed would lower the blood pressure.

Course.—The patient was transferred to the medical service for further observation. Urinary studies made there confirmed the presence of a mild degree of nephritis, an occasional hyaline cast being found. No interference with the elimination of phenolsulphonphthalein or evidence of nitrogen retention was detected. However, the headaches disappeared as the blood pressure fell to 120 systolic and 70 diastolic. The boy was discharged on July 12, 1928. He died at some time within the next nine months; details of the mode of death are not available.

CASE 5.—*History.*—M. H. B., a white woman, aged 48, who was admitted to the neurosurgical service of the University Hospital on March 9, 1929, complaining of headache and loss of vision, had commenced in December, 1925, to have menstrual disorders with a scanty but somewhat more frequent cycle. In June, 1926, the periods ceased entirely. She was in good health until January, 1928, when she experienced hot flashes and became dizzy. At that time, the blood pressure was reported to be 175 systolic. From January to June, 1928, she noted that she was becoming nervous and somewhat irritable. In July, 1928, severe headaches suddenly appeared, being localized first in the occipital region and then spreading forward all over the head. Within six weeks these headaches ceased, and during the fall of 1928 the hot flashes were again annoying and she was nervous and easily exhausted. In January, 1929, the headache abruptly returned and was accompanied by vomiting. At this time, she had two attacks of transient blindness, accompanied by unconsciousness and slight generalized convulsive movements. On January 14, vision in the left eye was markedly diminished, and a week later the acuity in the right eye became much impaired. Central vision was particularly affected, the peripheral fields being less involved. Some urinary frequency and urgency were noted at this time. On January 24, during an especially severe headache, the patient had a sensation of numbness and loss of power in the left hand. A second similar attack immediately preceded admission to the hospital.

Examination.—The patient was of a sallow complexion, lay quietly in bed, and was conscious and cooperative. The blood pressure was 175 systolic and 104 diastolic. There were two points in the occipital region of the head, to the right and left of the midline, which were acutely tender to pressure, and similar areas were present on each side of the neck over the trapezius muscles.

There was a slight bilateral exophthalmos. All ocular movements and reflexes were actively present. The media were clear to retinoscopic examination, the arteries small and white and lined with exudate, the veins engorged. Numerous small hemorrhages and patches of white, ill defined exudate were present about the disk. There was 2 diopters of choking on the right and 3 on the left. A slight horizontal nystagmus was noted, better defined on looking to the right than to the left. The other cranial nerves were normal. Suboccipital tenderness was present on moving the head.

There was no thyroid enlargement; the lungs were normal; the heart was somewhat enlarged to the left; the heart beat showed a marked sinus arrhythmia. In the aortic area, during respiration, there was heard a short blowing sound, which

was not heard during expiration or when the breath was held. The abdomen was normal. There was a generalized wasting of the muscles of the extremities. The reflexes were all normal; there was no clonus or Babinski sign. The gait was slightly ataxic, with widening of the base. Definite adiadokokinesis and ataxia were noted in the left hand, and awkwardness and uncertainty in movements of the left leg.

Laboratory studies showed a mild secondary anemia. Serologic tests of the blood and spinal fluid revealed nothing abnormal. The urine had a specific gravity varying from 1.009 to 1.015 and contained a trace of albumin and an occasional small hyaline cast. Lumbar puncture showed a pressure of 200 mm. of water and a clear fluid. Roentgen examination of the head gave negative results. Studies of the visual fields showed no cutting of the form fields, but a markedly enlarged blind spot, with complete loss of color fields in the left eye and of the temporal fields of the right eye. Visual acuity was 6/15 on the left and 6/30 on the right.

Course.—In spite of the presence of headache, vomiting and choked disk, with suggestive neurologic evidence of a left cerebellar tumor, the history was so clearly that of hypertension and renal disease that treatment was instituted along proper lines. Under rest in bed, a diet low in protein and eliminative measures the headache disappeared and vision improved. Although the blood pressure did not fall and the eyegrounds remained essentially unchanged, the patient was discharged on April 5, 1929. At present, her condition seems stationary, the headaches being much less frequent and the visual acuity somewhat increased.

INTRACRANIAL TUMOR WITH UNEQUAL CHOKED DISK

RELATIONSHIP BETWEEN THE SIDE OF GREATER CHOKING AND THE POSITION OF THE TUMOR *

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PHILADELPHIA

Though long a subject of controversy, the question of whether or not there is a significant relationship between the side of greater choking of the optic disk and the side of the tumor remains undecided. This question has considerable theoretical importance. It bears on the etiology of choked disk, and on the disturbances produced by expanding intracranial lesions.

Martin [1] studied 55 cases of intracranial tumor with unequal choked disk, and found that in the majority (71 per cent) the greater choking was on the same side as the tumor. Paton [2] studied 48 cases and found that in only 52 per cent was the greater choking on the same side as the tumor. He observed that tumors of the temporal lobe tended to give homolaterally greater choking more often than did tumors in other positions. Gunn,[3] analyzing Martin's data, had earlier made a similar observation.

MATERIAL AND METHOD

This study differs from previous ones in one essential, the number of cases studied. It is based on an analysis of 330 cases of tumor of the brain with unequal choked disk. This series was obtained by including from 2,200 cases of verified intracranial tumor, from the Johns Hopkins Hospital and the Peter Bent Brigham Hospital, only those

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1. Martin, J. M.: Optic Neuritis in Intracranial Tumors, Lancet **2**:81, 1897.

2. Paton, L.: Clinical Studies of Optic Neuritis in Its Relationship to Intracranial Tumors, Brain **32**:65, 1909.

3. Gunn, M.: Localisation of Intra-Cranial Tumours, Brain **21**:332, 1898.

showing unequal choked disk[4] before operation, and revealing at operation or at autopsy a localized primary intracranial neoplasm not crossing the midline.[5]

RESULTS

By referring to table 1 and figure 1 it may be seen that there was a notable excess of homolaterally greater choking among tumors in the temporal and parietal lobes. The incidence of contralaterally greater choking was higher among tumors in the occipital lobe than among tumors in other regions.

The incidence of homolaterally greater choking was higher among cases of frontal, parietal or temporal tumors with low grade choked disk than among similar cases showing high grade choked disk (fig. 2). The reverse was true of cases of tumor in the cerebellopontile angle or occipital lobe.

TABLE 1.—*Numerical Incidence of Homolaterally and of Contralaterally Greater Choking among Tumors in Different Regions*

	Johns Hopkins Series		Peter Bent Brigham Series		Combined Series	
Area	Homolateral	Contralateral	Homolateral	Contralateral	Homolateral	Contralateral
Frontal	29	17	40	22	69	39
Parietal	11	3	25	11	36	14
Temporal	13	3	33	12	46	15
Cerebellopontile angle	13	4	32	18	45	22
Occipital	5	4	10	12	15	16
Total	71	31	140	75	211	106

4. Unequal choked disk is used here to mean a difference in the amount of swelling or secondary atrophy of the two nerve heads. When no secondary atrophy was present, the side of greater swelling was considered the side of greater choking. When secondary atrophy was present, the side of greater atrophy was considered the side of greater choking. No cases were included in which it was reported that there was primary atrophy. I am aware of the difficulties involved in the measurement of swelling and atrophy of the nerve head. In this series there are undoubtedly cases in which the examiner erred. The assumption is made that errors tend to cancel themselves. Confidence in the accuracy of these records is strengthened by the knowledge that in a great number of cases the ophthalmologic examination was made independently by two examiners and that in only five such cases (which were discarded) was there a disagreement as to the side of the greater choking.

5. Because a discussion of homolaterality and of contralaterality is confused by the inclusion of cases of tumor involving both sides of the brain, cases of tumor of midline structures were discarded. Because of the difficulty of ascertaining from operative notes whether or not cerebellar tumors and tumors of the basal ganglia involved one or both sides of the brain, such cases were also discarded.

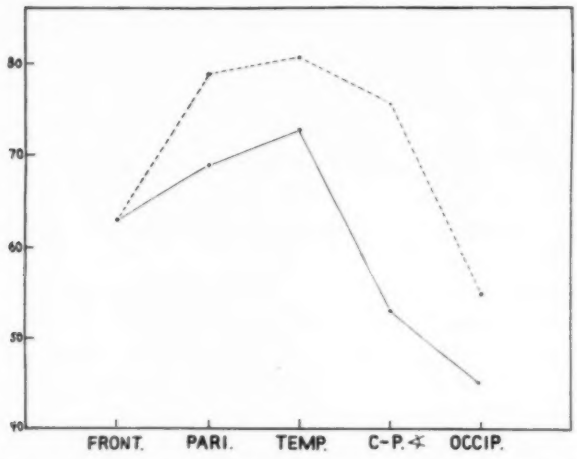

Fig. 1.—Percentage incidence of homolaterally greater choking among tumors in different regions. The dotted line indicates the Johns Hopkins Hospital series; the solid line, the Peter Bent Brigham Hospital series.

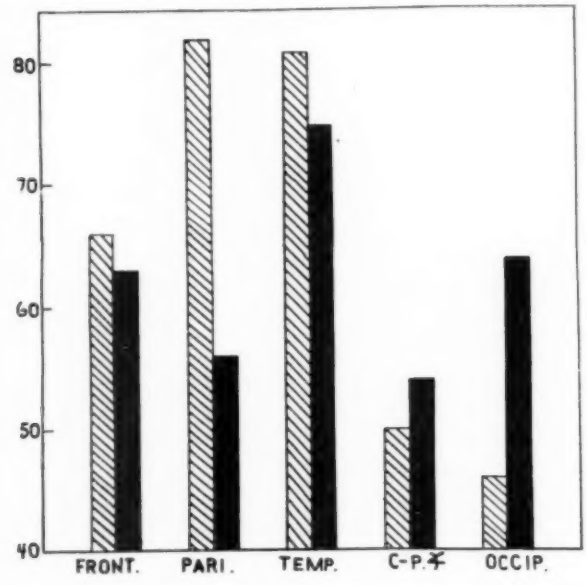

Fig. 2.—Percentage incidence of homolaterally greater choking in cases showing low grade choked disk (from 1 to 3 diopters [cross-barred columns]) and in cases showing high grade choked disk (from 4 to 10 diopters [solid black columns]), from the Peter Bent Brigham Hospital series.

The possibility that involvement of one of the cranial nerves is a factor in the production of unequal choked disk prompted an investigation of the association between the side of greater choking and the side of greater involvement of cranial nerves III to VII. As will be seen by referring to table 2, almost the same percentage of cases showed greater choking on the side opposite the greater involvement as on the side of the greater involvement.

COMMENT

From the analysis of this series it would seem that there is a definite relationship between the side of greater choking and the position of the tumor. Such a relationship argues against the importance of asymmetries not produced by the tumor. If one accepts the theory, suggested by Parker's [6] work, that a difference in intra-ocular pressure is of prime importance in producing unequal choked disk, one is forced to assume a mechanism by which tumors of the temporal and parietal lobes pro-

TABLE 2.—*Percentage of Cases Associated with Asymmetric Involvement of Cranial Nerves III to VII*

Cranial Nerve	Greater Choking Homolateral to Greater Involvement, per Cent	Greater Choking Contralateral to Greater Involvement, per Cent
V	11	10
VII	14	17
III, IV or VI	12	8

duce a lower intra-ocular pressure in the homolateral eye. Such a mechanism may exist, but it is not obvious. It does not appear to be associated with unequal involvement of cranial nerves III to VII (table 2). A relationship between the side of greater choking and the position of the tumor is not incompatible with the theory that involvement of trophic fibers to the nerve head influences the height of the edema, but the existence of such trophic fibers has not been proved. Those who advance the idea that unequal choked disk is a result of a difference in pressure of the cerebrospinal fluid in the sheaths of the optic nerves must assume a fluid-tight barrier between the two sides of the chiasm; this is not an easily accepted assumption. It is granted that compression of the sheath of one optic nerve might prevent pressure of cerebrospinal fluid from acting on the nerve head on that side, and as a result choking might be greater on the opposite side. This does not, however, appear to be the usual way in which contralaterally greater

6. Parker, W. R.: Relation of Choked Disk to the Tension of the Eyeball, J. A. M. A. **67**:1053 (Oct. 7) 1916; Mechanism of Papilledema, Arch. Neurol. & Psychiat. **14**:31 (July) 1925.

choking is produced, for the highest incidence of contralaterally greater choking occurred among tumors in the occipital lobe and in the cerebellopontile angle, that is, among tumors not at all well situated for pressing on the sheath of one optic nerve.

Swift [7] explained unequal choked disk in tumor of the brain as due to unequal interference with venous drainage from the two nerve heads. His explanation involves the following assumptions: (1) that interference with venous drainage from the nerve head is a factor of etiologic importance in choked disk, (2) that compression of certain veins and sinuses produces a rise of venous pressure in the central vein of the retina and in the veins of the nerve head, (3) that a tumor, as it grows, compresses adjacent veins and sinuses and (4) that the rise of

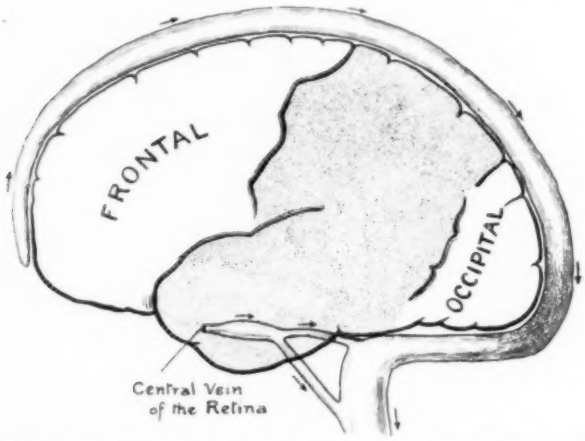

Fig. 3.—Relation between the intracranial venous channels that drain the nerve head and the regions in which tumors showed the greatest tendency to produce homolaterally greater choking. The stippled area indicates the regions in which tumors most frequently produced homolaterally greater choking. They lie directly above the venous channels draining the nerve head.

pressure is not always the same in both nerve heads, that it is often sufficiently different to produce a difference in choking in the two eyes.

According to Swift's theory one would expect to find tumors producing homolaterally greater choking grouping above the intracranial vessels that drain the nerve head (fig. 4). Figure 3 indicates that this is the case.

It is interesting to speculate as to whether the relatively high incidence of contralaterally greater choking among occipital tumors is to

7. Swift, G. W.: Choked Disk in Intracranial Lesions: Mechanical Factors in Its Causation, Northwest Med. **26**:579, 1927; The Transverse Sinus and Its Relation to Choked Disk, Arch. Ophth. **3**:47 (Jan.) 1930.

be explained by a greater rise in venous pressure in the contralateral nerve head as a result of the tumor compressing the lateral sinus (fig. 5).

One might account for the lower incidence of homolaterally greater choking among temporal and parietal tumors with low grade choked disk as compared with high grade choked disk (fig. 2) by assuming that

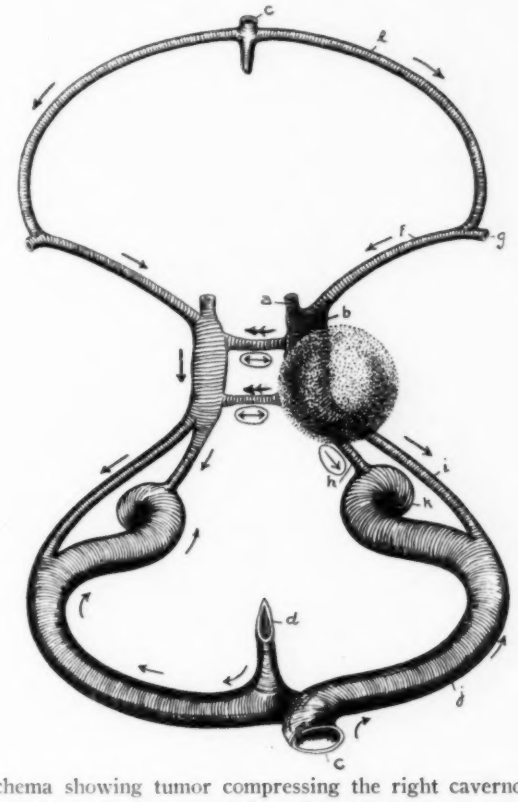

Fig. 4.—Schema showing tumor compressing the right cavernous and petrosal sinuses, with resulting disturbance of flow through the large venous channels at the base of the brain. A single-headed arrow indicates the normal direction of flow; a double-headed arrow, an abnormal direction of flow; an arrow with a line around it, normal flow that has been abolished. Darkly shaded vessels are those in which pressure is increased; *a* indicates the ophthalmic vein and central vein of the retina; *b*, the cavernous sinus; *c*, the superior sagittal sinus; *d*, the straight sinus; *e*, the inferior frontal vein; *f*, the sphenoparietal sinus; *g*, the external sylvian vein; *j*, the lateral sinus, and *k*, the jugular bulb. Normally, venous blood from the nerve head drains into the homolateral cavernous sinus by way of the central vein of the retina. Interference with flow through the cavernous sinus would raise the pressure in the central vein. The rise in pressure and the consequent interference with drainage from the nerve head would be greater on the side homolateral to the obstruction.

when such tumors reached a size sufficient to produce high grade choked disk, they had become somewhat more occipital and therefore less likely to produce homolaterally greater choking, and that when occipital tumors and tumors of the cerebellopontile angle reached a size sufficient

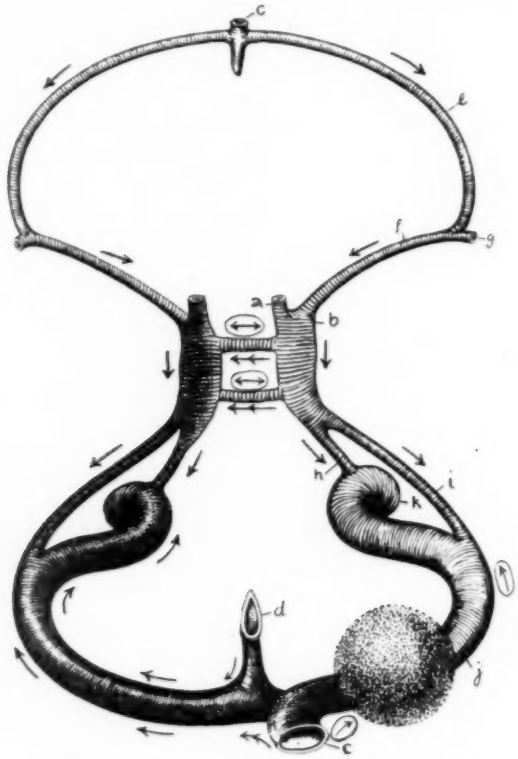

Fig. 5.—Schema showing tumor compressing the right lateral sinus, with resulting disturbance of flow through the large venous channels at the base of the brain. A single-headed arrow indicates the normal direction of flow; a double-headed arrow, an abnormal direction of flow; an arrow with a line around it, normal flow that has been abolished. Darkly shaded vessels are those in which pressure would be increased; *a* indicates the ophthalmic vein and central vein of the retina; *b*, the cavernous sinus; *c*, the superior sagittal sinus; *d*, the straight sinus; *e*, the inferior frontal vein; *f*, the sphenoparietal sinus; *g*, the external sylvian vein; *j*, the lateral sinus, and *k*, the jugular bulb. Normally, venous blood from the nerve head drains into the homolateral cavernous sinus by way of the central vein of the retina. Compression of the right lateral sinus would cut off flow usually contributed to the right jugular bulb. This would reduce the pressure in the right jugular bulb. Pressure in the right petrosal sinuses and right cavernous sinus would be reduced. Drainage from the right nerve head would be facilitated. Dammed-up flow through the right lateral sinus would be shunted in part to the left lateral sinus. This would increase the pressure in the left lateral sinus, and would interfere with flow from the left petrosal sinuses and the left cavernous sinus. Drainage from the left nerve head would be impaired.

to produce high grade choked disk, they had become somewhat more parietotemporal and therefore more likely to produce homolaterally greater choking.

All the observations recorded can be fitted into Swift's theory. An attempt will be made to check the correctness of the theory experimentally.

CONCLUSIONS

In cases of tumor of the brain with unequal choked disk:

1. Greater choking tends to occur on the same side as the tumor.

2. The incidence of homolaterally greater choking is highest among tumors of the temporal and parietal lobes.

3. The incidence of contralaterally greater choking is highest among occipital tumors.

4. The incidence of homolaterally greater choking is higher among cases of parietal tumor with low grade choked disk than among similar cases with high grade choked disk.

5. The incidence of homolaterally greater choking is lower among cases of occipital tumor with low grade choked disk than among similar cases with high grade choked disk.

6. There is no significant association between the side of greater choking and the side of greater involvement of cranial nerves III to VII.

INTERNAL JUGULAR VENOUS PRESSURE IN MAN

ITS RELATIONSHIP TO CEREBROSPINAL FLUID AND CAROTID ARTERIAL PRESSURES *

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We undertook to measure the venous pressure of the internal jugular vein near the bulb and to correlate this pressure with the cerebrospinal fluid pressure. Since there are three factors in intracranial dynamics, first, the arterial pressure, second, the venous pressure and third, the cerebrospinal fluid pressure, we also undertook in a few cases to measure the intracarotid pressure and to note its relationship under experimental conditions to the jugular venous and the cerebrospinal fluid pressures. Practically all of the previous work on the important subject of the relation of the venous and cerebrospinal fluid pressures has been done on animals under conditions of anesthesia. Our object was to study the various pressures mentioned in the human being under experimental and clinical conditions. It is obvious that it is impossible to trephine into the torcular Herophili in a human being, and that the introduction of a cannula in the carotid artery of a patient would be looked on askance even by the most hardened research worker. Further, ether directly changes conditions in the brain so that the animal experiments have this added factor to complicate an already difficult situation.

TECHNIC

In the main, we devoted ourselves to a comparative study of the jugular venous pressure and the cerebrospinal fluid pressure as measured by the internal jugular puncture and by the ordinary lumbar puncture route. Theoretically, our cerebrospinal fluid pressure should be measured by either cisternal or ventricular puncture. Unfortunately, it is impossible to obtain permission for cisternal or ventricular puncture at the State Hospital where we operate. We are forced to use the lumbar puncture route as our way of measuring cerebrospinal fluid pressure and to make certain deductions from its rise and fall from the experiments recorded in the literature.

The lumbar puncture was done in the ordinary way with the pressure recorded by an Ayer manometer. The standard horizontal position of the body and head

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* From the Research Division, Boston State Hospital and the Department of Neurology, Tufts College Medical School.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

was used, and the middle line between the second and third or the third and fourth lumbar vertebrae was taken as the puncture site.

Description of the Jugular Puncture.—The internal jugular vein is selected as it courses near the tip of the mastoid on its way downward from the jugular foramen. At this point the vessel is large, fairly constant in position and very close to the skull and receives no tributaries from the face or neck, and thus its content represents pure brain blood. This technic has been described elsewhere in the literature,[1] but a redescription, especially in view of the difficulties of measuring the venous blood pressure, is necessary.

The best position of the head and neck for this puncture is with the patient on his side, the opposite side of the face well supported by a pillow and the head somewhat extended on the neck. A needle of 18 gage and 40 mm. in length is thrust into the tissues of the neck, which have been well anesthetized, at the juncture of the tip of the mastoid with the anterior border of the sternocleidomastoid muscle. The point of the needle is slid over the tip of the mastoid and thrust perpendicularly into the tissues of the neck to its full extent. It is then slowly withdrawn, suction being made on a Luer syringe that is attached to the needle. As the needle is slowly withdrawn, the venous blood of the jugular vein is drawn into the syringe. The syringe is immediately disconnected, and an Ayer manometer such as is used for measuring cerebrospinal fluid pressure is connected with the needle and held perpendicularly to the side of the neck.

Clotting in the needle is the one great difficulty of the experiment. To avoid this, an absolutely clean, smooth and rustless needle is necessary, and it is advisable to flood with potassium citrate. We have found that a platinum needle is the only safe type to use, since with steel needles clotting occurs much more readily. The inside of the manometer is also moistened with citrate. When clotting commences, the experiment is finished, since it is then impossible to rely on the results obtained.

A perfect technic in obtaining the blood is essential for the pressure experiments, although it is not at all essential for such experiments as we have previously reported in biochemical studies.

The needle should penetrate the vein in the first attempt; otherwise, serum and other substances enter the needle and somehow facilitate clotting. If the needle is properly introduced and is perfectly clean, then by good fortune an experiment can be kept going for from five to ten minutes. We have never succeeded in keeping the blood in the manometer and needle unclotted for a longer time than ten minutes, but generally the experiment is over in five minutes. It is advisable to do the lumbar puncture first, to register its pressure, and then to do the jugular puncture. The venous pressure of the jugular vein is seen to respond to respiration, and this oscillation is a guide as to whether or not the blood has clotted.

THE COMPARATIVE PRESSURE OF THE INTERNAL JUGULAR VENOUS PRESSURE AND THE CEREBROSPINAL FLUID PRESSURE

Among the twenty-eight cases that we studied, all of which were from the Boston State Hospital and represent cases of dementia praecox, dementia paralytica and cerebral arteriosclerosis, there were no cases of increased intracranial pressure, and we also avoided for our

1. Myerson, A., and Halloran, R. D.: Technic for Obtaining Blood from the Internal Jugular Vein and the Internal Carotid Artery, Arch. Neurol. & Psychiat. **17**:807 (June) 1927.

preliminary work any cases in which there were marked heart disease, decompensation, etc. The comparison between the internal jugular venous pressure and the cerebrospinal fluid pressure is shown in table 1. It will be seen that the cerebrospinal fluid pressure is greater in all but two cases. In these two it was impossible to read either the jugular venous pressure or the cerebrospinal fluid pressure, both being too low to record. That these two cases did not represent artefacts or failures of technic is shown by the fact that on jugular compression the cerebrospinal fluid and jugular venous pressures rose. The range of difference between the two pressures is quite extraordinary, as is seen by the table. In some cases they seem to be almost equal; in others, the difference is 110 mm. of water. We have not as yet been able to discover what conditions are responsible for the range of difference

TABLE 1.—*Relationship of Cerebrospinal Fluid and Internal Jugular Pressures in the Horizontal Position in Twenty-Eight Cases* *

Patient	C.F.P. in Mm. of Water	I.J.P. in Mm. of Water	Difference	Patient	C.F.P. in Mm. of Water	I.J.P. in Mm. of Water	Difference
J. S.	80	70	10	J. M.	155	70	85
F. E.	140	120	20	H. V.	100	80	20
R. B.	100	70	30	B. H.	0	0	0
J. H.	150	140	10	F. H.	170	70	100
R. B.	90	80	10	J. M.	110	80	30
T. K.	170	90	80	B. H.	85	40	45
M. G.	150	135	15	F. H.	190	75	115
J. M.	110	90	20	M. M.	85	40	45
M. D.	110	90	20	J. H.	0	0	0
J. T.	140	30	110	H. S.	60	0	60
N. C.	180	115	65	F. T.	160	90	70
M. G.	140	80	60	W. B.	150	40	110
A. F.	140	75	65	A. F.	110	70	40
A. F.	100	90	10	M. M.	70	40	30

* In this and the succeeding tables, C.F.P. indicates cerebrospinal fluid pressure and I.J.P., internal jugular pressure.

between the two pressures. It may be that our technic is not as yet perfect. Since the internal jugular vein is on the road to the heart from the brain, it necessarily follows that the pressure recorded by our method is lower than that which would be obtained in the skull. It is therefore impossible to draw any incontestable conclusions from our experiments as to whether or not the cerebrospinal fluid pressure is greater than that of the cerebral venous pressure. On the whole, our experiments did indicate that very likely the cerebrospinal fluid pressure is greater,[2] since it is impossible to conceive that in some cases

2. For contradictory views on this matter see: Becht, F. C.: Studies in Cerebrospinal Fluid, Am. J. Physiol. **51**:1, 1920. Hill, L.: The Physiology and Pathology of Cerebral Circulation, London, J. & A. Churchill, 1896. Weed, L. H., and Hughson, W.: Intracranial Venous Pressure and Cerebrospinal Fluid Pressure, Am. J. Physiol. **58**:101, 1921. Weed, L. H.: Experimental Studies in Intracranial Pressure, Association for Research in Nervous and Mental Diseases, 1927. Howe, H. S.: Physiologic Mechanism for the Maintenance of Intracranial Pressure, Arch. Neurol. & Psychiat. **20**:1048 (Nov.) 1928.

110 mm. of difference between the internal jugular vein and the torcular Herophili exists. There is no exact comparison possible between the pressure conditions within the internal jugular vein outside the skull and the sinuses from which it arises in the rigid skull. In the neck, the vein may be held in some degree of tension by the muscle tissue around it.

TABLE 2.—*Effect of Jugular Compression on Cerebrospinal Fluid and Internal Jugular Pressures*

Patient		Initial Pressure	Jugular Compression	Ratio of Rise
A. F.	C.F.P.	100	580	5.8
	I.J.P.	90	460	5.1
R. B.	C.F.P.	100	350	3.5
	I.J.P.	70	440	6.3
J. H.	C.F.P.	0	160	...
	I.J.P.	0	160	...
A. F.	C.F.P.	140	350	2.5
	I.J.P.	75	290	3.9
A. Fuk.	C.F.P.	110	310	2.8
	I.J.P.	70	290	4.1
J. S.	C.F.P.	80	340	4.2
	I.J.P.	70	280	4.0
J. H.	C.F.P.	150	350	2.3
	I.J.P.	140	340	2.4
P. D.	C.F.P.	40	175	4.3
	I.J.P.	80	290	3.6
B. H.	C.F.P.	85	200	2.3
	I.J.P.	40	150	3.7
N. Br.	C.F.P.	150	420	2.8
	I.J.P.	40	240	6.0
F. E.	C.F.P.	140	450	3.2
	I.J.P.	120	270	2.3
R. B.	C.F.P.	90	350	3.8
	I.J.P.	80	440	5.5
N. C.	C.F.P.	180	350	1.9
	I.J.P.	115	250	2.1
A. F.	C.F.P.	250	400	1.6
	I.J.P.	130	230	1.7
F. H.	C.F.P.	170	340	2.0
	I.J.P.	70	155	2.2

THE EFFECTS OF JUGULAR COMPRESSION ON THE CEREBROSPINAL FLUID PRESSURE AND THE INTERNAL JUGULAR VENOUS PRESSURE

On compressing the neck in the ordinary Queckenstedt manner, the jugular venous pressure rises promptly and falls promptly, this rise and fall being synchronous with the rise and fall of the cerebrospinal fluid pressure. We here append a few experiments in which this was done (table 2). It will be noted that there is no exact correspondence between the magnitude of the rise and fall of the venous pressure and the rise and fall of the cerebrospinal fluid pressure. This we believe is probably due to imperfect technic, since the variability in the results

follows no rule and may in part be due to the fact that our patients did not always take kindly to compression of the neck, being easily frightened and often somewhat resistive. When the patients were quite cooperative and not emotional or resistive, the two pressures had about the same ratio of fall and rise.

In a patient to whom we gave ether and whose case will be recorded in detail later, the cerebrospinal fluid pressure was 250 mm. and the jugular venous pressure was 130 mm. prior to the compression of the neck. With the Queckenstedt compression, the cerebrospinal fluid pressure rose to 400 mm. and the jugular venous pressure rose to 230 mm., which is an approximately equivalent ratio of the increase of both. We have not had any cases of cerebrospinal fluid block. It

TABLE 3.—*Effect of Abdominal Pressure on Cerebrospinal Fluid and Internal Jugular Pressures*

Patient		Initial Pressure	Abdominal Pressure	Ratio of Rise
F. E.	C.F.P.	170	460	2.7
	I.J.P.	40	200	5.0
N. C.	C.F.P.	180	270	1.5
	I.J.P.	115	260	2.2
R. B.	C.F.P.	100	290	2.9
	I.J.P.	70	110	1.6
A. Fal.	C.F.P.	110	225	2.0
	I.J.P	70	290	4.1
J. S.	C.F.P.	80	200	2.5
	I.J.P.	70	140	2.0
A. F.	C.F.P.	140	270	1.9
	I.J.P.	75	150	2.0
J. M.	C.F.P.	150	190	1.2
	I.J.P.	140	195	1.4
F. H.	C.F.P.	170	270	1.6
	I.J.P.	70	115	1.6

would no doubt be interesting to see the jugular venous pressure rise when the cerebrospinal fluid pressure did not, and thus one would get one added confirmation of block.

COMPRESSION OF THE ABDOMEN AND OTHER EXPERIMENTS

Abdominal compression (table 3) shows a rise in the cerebrospinal fluid pressure and a rise in the jugular venous pressure. Our results by this technic are somewhat irregular. Since abdominal pressure is an unsatisfactory procedure in the conscious human being, all that one can safely state is that this technic raises both the venous pressure and the cerebrospinal fluid pressure.

Coughing, straining as if at stool and loud talking (table 4) raise both the cerebrospinal fluid pressure and the jugular venous pressure. It is interesting to see this pressure rise on talking. Straining as if at stool raises the cerebrospinal fluid pressure remarkably and sends the

jugular venous pressure up in increasing measure. As we shall show later, it also sends up the carotid arterial pressure, so that a constipated stool creates an increase in the arterial pressure within the brain as well as in the venous pressure and that of the cerebrospinal fluid. Just what happens under these circumstances is not known, but it is common for people who are constipated and strain at stool to suffer from severe headache as a result of the efforts. It is also noteworthy that a good many cerebral hemorrhages take place when the patient is straining at stool. The early morning coming-from-the-stool "shock" may perhaps be explained on the basis of this rise in arterial and cerebrospinal fluid pressure. The danger for the elderly orator and for any one engaged in violent expiratory and straining effort who has cerebral arteriosclerosis seems evident from our observations.

TABLE 4.—*Effect of Various Acts on the Cerebrospinal Fluid and Internal Jugular Pressures*

Patient		C.F.P.	Ratio of Rise	I.J.P.	Ratio of Rise
W. B.	Initial pressure	150	...	40	...
	Jugular compression	420	2.8	240	6.0
	Coughing	350	2.5	100	2.5
	Straining	330	2.3	120	3.0
A. F.	Initial pressure	110	...	70	...
	Jugular compression	310	1.9	290	4.1
	Abdominal pressure	225	2.0	290	4.1
	Coughing	150	1.3	100	1.3
B. H.	Initial pressure	85	...	40	...
	Compressing chest	180	2.1	130	3.2
	Coughing	250	3.0	100	2.5
	Talking	150	1.9	60	1.5
M. M.	Initial pressure	70	...	40	...
	Jugular compression	280	4.0	200	5.0
	Abdominal pressure	220	3.1	150	3.7
	Coughing	240	3.4	150	3.7

THE EFFECT OF POSTURE

At this point it is necessary to describe our carotid arterial pressure experiments in order to link them up with the observations on the effect of posture.

The common carotid artery has been clinically punctured for some time, mainly for therapeutic purposes.[3] A paper, which is to be published soon, by William Dameshek and one of us (Dr. Loman), describes a technic for studying intra-arterial pressure. In accordance with this technic, the carotid artery was punctured by an 18 gage needle to which was attached a glass trap containing citrate, and this trap was connected with an ordinary aneroid manometer. The intra-arterial pressure is thus recorded. It must be stated, that the pressure recorded is neither at systole nor at diastole, but at a mean between the two.

3. Hirsch, H. L.; Myerson, A., and Halloran, R. D.: Intracarotid Treatment of General Paresis, Boston M. & S. J. **192**:713, 1925. Also see this paper for other references.

In the main, we divided our experiments in regard to the effect of posture into two groups: in one we made a simultaneous comparison between the lumbar puncture and the jugular venous pressure (table 5), and in the other (table 6), a comparison between the jugular venous pressure and the carotid pressure. It has been shown by animal experi-

TABLE 5.—*Effect of Posture on Cerebrospinal Fluid and Internal Jugular Pressures* *

Patient		Horizontal	Head Down	Head Up	Range†
A. F.	C.F.P.	100	65	240	175
	I.J.P.	90	130	0	130
W. V.	C.F.P.	100	60	250	190
	I.J.P.	80	140	70	70
F. E.	C.F.P.	140	90	270	180
	I.J.P.	120	150	60	90
N. C.	C.F.P.	180	130	200	70
	I.J.P.	115	155	70	85
M. G.	C.F.P.	140	50	180	130
	I.J.P.	80	120	0	120
H. G.	C.F.P.	140	70	270	200
	I.J.P.	60	115	40	75
M. H.	C.F.P.	0	0	260	260
	I.J.P.	0	140	0	140
J. S.	C.F.P.	80	0	220	220
	I.J.P.	70	110	0	110
A. F.	C.F.P.	140	115	180	65
	I.J.P.	75	110	60	50
H. H.	C.F.P.	190	130	350	220
	I.J.P.	75	120	0	120

* The body was lowered and raised at a 45 degree angle from the horizontal level.
† Between head up and head down positions.

TABLE 6.—*Effect of Posture on Cerebrospinal Fluid and Carotid Pressures*

Patient		C.C.P.,* in Mm. Hg	Change in Pressure, in Mm. Water	I.J.P.	Change in Pressure, in Mm. Water
D. F.	Initial pressure	90	...	40	...
	Head down	100	135	120	80
	Head up	84	81	10	30
W. B.	Initial pressure	80	...	50	...
	Head down	98	243	150	100
	Head up	70	135	10	40
H. H.	Initial pressure	94	...	75	...
	Head down	102	108	160	85
	Head up	84	135	40	35

* C.C.P. indicates common carotid pressure.

ments [4] that the intracranial cerebrospinal fluid pressure during changes of posture is just the reverse of the lumbar puncture cerebrospinal fluid pressure. This is easily understood since, when the head is elevated, the weight of the column of the cerebrospinal fluid is greatest at the lumbar puncture site, and not within the brain itself. Exactly the reverse follows when the head is lowered. When the head is

4. See works of Hill, Weed and Hughson, Becht and Howe (footnote 2).

raised, the jugular venous pressure drops below zero. The lumbar puncture cerebrospinal fluid pressure rises higher, but, as has been stated before, in such cases when pressure is recorded by the cisternal method it is correspondingly low. In other words, the intracranial cerebrospinal fluid pressure and the internal jugular venous pressure both drop with the sitting up position or with the head elevated. When the head is lowered, the internal jugular pressure rises immediately. A few experiments are here recorded (table 5).

Ernstene and Blumgart,[5] in a recent paper, in experimenting on the sitting up posture that the orthopneic patient takes, stated that the venous pressure is thereby lowered and consequently the capillary pressure is relieved and as a result the respiratory center operates better. They did not measure the jugular venous pressure, but our measurements confirm their theoretical conclusions completely.

A very interesting observation was recorded in the pressure within the carotid artery on a change of posture. Table 6 shows what happened in several of our cases. As the head is raised (which, by the way, must be done very cautiously, with the pressure apparatus continually held in the same general relationship to the moved head and neck, in order to avoid the slipping out of the needle), the carotid artery pressure first drops and then, with the head still held up, the pressure gradually reaches the level recorded with the horizontally held head. There seems to be a mechanism that tends to bring the arterial pressure back to the horizontal level on a change of posture. The rise of pressure in the carotid artery is as great or greater than that which takes place in the spinal fluid and the jugular vein, since the fluctuation may be as much as from 20 to 30 mm. of mercury as against 250 mm. of water. Thus, when the head is raised, all the factors that make for the pressure within the head, namely, the arterial pressure, the venous pressure and the cerebrospinal fluid pressure, drop. When the head is lowered these same pressures rise. We believe that there is a practical application somewhere of these facts to sleep, to certain types of headache, etc. It may be noted also that violent expiratory efforts of any type raise all these three components of intracranial pressure, whereas deep inspiration and relaxation lower all these pressures.

In the literature it is unanimously agreed that while the arterial pressure is a factor in cerebrospinal fluid pressure, the latter is directly related to the cerebral venous pressure; that the rise and fall are in direct correspondence with this latter pressure, and that only indirectly are they related to the arterial pressure. Our experiments corroborate

5. Ernstene, A. C., and Blumgart, H. L.: Orthopnea: Its Relation to the Increased Venous Pressure of Myocardial Failure, Arch. Int. Med. **45**:593 (April) 1930.

this point of view so far as certain physical situations are concerned, though our later experiments bring to light quite different relationships, and we may consolidate our experiments by the following statements:

When the patient sits up or lies down, the fall and rise of the cerebrospinal fluid pressure and venous pressure are accompanied by a corresponding rise of arterial pressure. Thus, in the cases recorded (tables 6 and 7) it will be seen that the arterial rise and fall are even greater when translated into terms of water pressure than the changes in cerebrospinal fluid pressure and jugular venous pressure.

It is also true that on straining, as at stool, on coughing, etc. (table 7), the arterial pressure also rises with the venous and cerebrospinal fluid pressures. In other words, these situations and acts, namely, those of posture and violent respiratory effort, simultaneously alter the whole

TABLE 7.—*Simultaneous Cerebrospinal Fluid, Internal Jugular and Intracarotid Pressures; Effect of Various Acts*

Patient		C.F.P.	Actual Rise, in Mm. Water	I.J.P.	Actual Rise, in Mm. Water	C.C.P.,* in Mm. Hg	Actual Rise, in Mm. Water
W. B.	Initial pressure	150	...	40	...	80	...
	Coughing	350	200	100	60	102	297
	Head down	...	...	150	110	98	243
	Straining	330	180	120	80	106	351
B. H.	Initial pressure	85	...	40	...	84	...
	Compressing chest	180	105	100	60	94	135
	Coughing	250	165	80	40	96	162
	Talking	150	65	70	30	90	87
	Head down	...	...	100	60	98	189

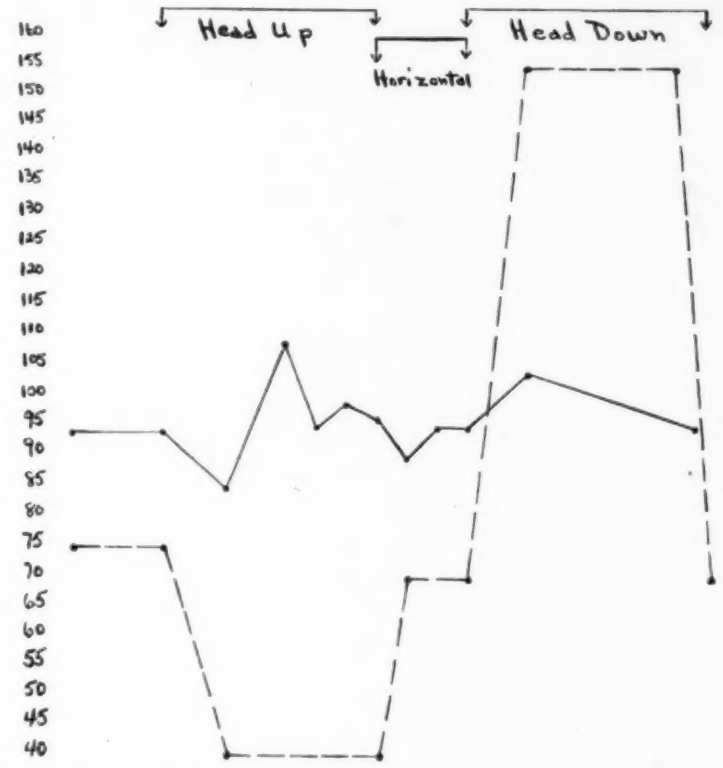
* C.C.P. indicates common carotid pressure.

complex of intracranial dynamics, namely, the arterial pressure, the venous pressure and the cerebrospinal fluid pressure. It does not of course follow, however, that the venous and the cerebrospinal fluid pressures are dependent on the rise or fall of the arterial pressure.

That this is not the case in the human being is shown by the following experiments:

An Experiment Performed Under Ether Anesthesia.—Before ether was administered, the subject, a man who had dementia praecox and was very thin and quite deteriorated both mentally and physically, was found to have a cerebrospinal fluid pressure of 140 mm. and a jugular venous pressure of 75 mm. The arterial pressure directly measured at the arm was 100 systolic and 70 diastolic; the pulse rate was 102 per minute. We have no way of comparing this arterial pressure with the intracarotid pressure, since in this experiment we did not examine the latter pressure. He was given ether to the point of complete relaxation. The cerebrospinal fluid pressure rose to 250 mm.; the jugular venous pressure rose to 130 mm. In other words, there was a corresponding rise in both the cerebrospinal fluid pressure and the jugular venous pressure. On bilateral compression of the neck, the cerebrospinal fluid pressure rose to 400 mm., and the venous pressure

rose to 230 mm. During the course of the experiment, the patient's condition became poor, the blood pressure suddenly falling to 68 systolic and 30 diastolic, the pulse rate then being 76. Nevertheless, while the blood pressure was falling the cerebrospinal fluid pressure and the venous pressure practically remained unaltered. At the end of the experiment the cerebrospinal fluid pressure was 240 mm. and the venous pressure 120 mm., an inconsequential dropping and one that represented the up and down fluctuations of the experiment rather than any actual change. In other words, under ether the venous pressure rose as did the cerebrospinal fluid pressure. The arterial pressure did not rise, although the pulse rate



Effect of postural changes on the intracarotid and internal jugular pressures. The continuous line indicates the common carotid pressure (in millimeters of mercury); the broken line, the internal jugular pressure (in millimeters of blood).

increased. With a fall of blood pressure during the experiment and slowing of the pulse, there was no essential change in the cerebrospinal fluid or the cerebral venous pressure.

An Experiment with Amytal.—An experiment with amytal showed first that amytal does not increase the intracranial pressure as does ether. At the beginning of the experiment, the blood pressure was 126 systolic and 80 diastolic; the jugular venous pressure was zero; that is, there was no pressure recorded; the cerebrospinal fluid pressure was 60 mm., a low pressure. This patient was recovering

from alcoholic multiple neuritis. The blood pressure remained the same for a short time. The jugular pressure and cerebrospinal fluid pressure remained unaltered. The blood pressure then dropped to 106 mm. The jugular venous pressure and the cerebrospinal fluid pressure remained unaltered. In other words, in this case with a normal blood pressure there was a low cerebrospinal fluid pressure and a low venous pressure, showing a lack of relationship. Furthermore, the anesthesia caused no essential changes in pressure conditions, differing very remarkably in this respect from ether. With a fall of blood pressure there was no change in the cerebrospinal fluid or in the jugular venous pressure. It is probable that the jugular venous pressure depends, as all venous pressure does, more on the state of the capillaries than on the state of the arteries; that when the capillary pressure is high, the venous pressure is high; that when the capillary pressure is low, the venous pressure is low, and that the relationship of cerebrospinal fluid pressure and venous pressure depends more on the capillary pressure than on the gross arterial pressure.

Another experiment that bears on this relationship between arterial pressure and venous pressure was performed as follows: A needle was thrust into the common carotid artery and connected with the aneroid manometer, as previously described. The internal jugular venous pressure was also recorded. As will be seen from the accompanying chart, the carotid pressure dropped when the patient's head was raised, rose higher than the horizontal pressure and gradually came down to about the horizontal level, whereas, during these changes, the jugular pressure dropped and remained at a constant level. When the head was lowered to its original position, there was a fall in the intracarotid pressure to below the horizontal pressure, with the gradual assumption of the original pressure. During this time the internal jugular pressure had returned to slightly below its original horizontal pressure and remained constant there. When the head was lowered, there was a sudden rise in the intracarotid pressure with a gradual fall. Simultaneously the internal jugular pressure increased and remained stationary. In other words, while the arterial pressures under postural changes fluctuated, the venous pressures remained constant.

There seems to be some mechanism for reestablishing arterial pressure but none that operates so directly on venous pressure, venous pressure being more a function of posture than is arterial pressure.

We believe that this preliminary paper establishes definitely that intracranial dynamics can be studied in the human being in a safe and scientific manner, and that it opens the way to a more intensive study of the changing pressure conditions in the brain in the various clinical situations.

TRAUMATIC SUBDURAL HEMATOMA

WITH PARTICULAR REFERENCE TO THE LATENT INTERVAL *

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Traumatic subdural hematoma is a definite clinical entity that has been given considerable attention in the medical literature since Virchow's classic description [1] of "hematomas of the dura mater" in 1857. The lesion consists of an encysted collection of blood, situated between the dura and the arachnoid membranes, usually over the convexity of the cerebral hemisphere. It is my aim to sketch briefly the clinical and pathologic aspects of this interesting lesion and to dwell particularly on the reason for its delayed clinical manifestations.

The majority of published reports of cases of traumatic subdural hematoma are similar in one respect, that is, in the occurrence of a latent interval between the reception of trauma and the onset of pressure symptoms. The cranial trauma that was responsible may have been severe or so trivial as to be readily forgotten. In many instances a history of trauma that had been denied previously has been obtained after operative verification of the lesion has led to closer questioning of the patient or his relatives. The latent interval may vary from a few hours to many months or even years, and during this period the symptoms may be slight or even entirely absent.

The onset of symptoms may be insidious or rapidly progressive. The most common symptom is headache, occasionally associated with vomiting. Mental disturbances occur more frequently in the presence of this condition than in the case of any other space-filling intracranial lesion. Inequality of the pupils, papilledema and pyramidal tract signs are frequently present. Convulsions, either jacksonian or generalized, may occur. However, lateralizing signs are not of great significance, since the lesion is often found on the side opposite to that which is indicated by the symptoms. In a certain percentage of cases the lesion is bilateral.

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* From the Cleveland Clinic.

* Read before the Section on Nervous and Mental Diseases at the Eighty-Second Annual Session of the American Medical Association, Philadelphia, June 12, 1931.

1. Virchow, R.: Das Hämatoma der Dura mater, Verhandl. d. phys.-med. Gesellsch. **7**:134, 1857.

During the past few years, seven cases of traumatic subdural hematoma have been studied in the neurosurgical department of the Cleveland Clinic Hospital. Five of the patients recovered following an operation, while two died with the condition undiagnosed (fig. 1). The following case is a fairly typical one.

REPORT OF A CASE

History.—A man, aged 52, was admitted to the Cleveland Clinic on Feb. 4, 1930, with lapse of memory as the chief complaint. On Dec. 12, 1929, he had driven his automobile into a ditch, colliding with a concrete culvert. He was

Fig. 1.—Postmortem specimen of bilateral subdural hematoma.

unconscious for about an hour and a half. On regaining consciousness he did not recall events that had occurred for approximately ten minutes prior to the accident. He sustained a small laceration over the left eye. He remained at home for four weeks, during which time he did not feel himself; after this he resumed work as a certified public accountant, feeling that he was entirely well. Three weeks later, he had a period of complete amnesia lasting for forty-eight hours. For this reason he was referred to the clinic by Dr. Paul Zinkham, of Ravenna, Ohio.

Examination.—The patient was alert mentally and apparently in good health; the temperature was normal, the pulse rate, 88, and the blood pressure, 126 systolic and 90 diastolic. The ocular fundi presented an early papilledema. Roentgen examination of the skull gave negative results for any evidence of fracture. Neurologic examination gave negative results. The spinal fluid pressure

was 240 mm. of water. The fluid was clear and colorless and contained 2 cells. The Wassermann and colloidal gold reactions were negative.

Course.—Forty-eight hours after admission, the patient lapsed into semistupor, and a complete paralysis of the left third nerve developed, with a slight weakness in drawing up the right corner of the mouth. The pulse rate was 48, and the blood pressure, 188 systolic and 144 diastolic. An immediate operation was decided on, the preoperative diagnosis being intracranial hemorrhage.

Operations.—Since the symptoms indicated a lesion on the left side, the usual subtemporal decompression was performed on that side. Except for increased intracranial pressure, the observations at the operation were entirely negative. Forty-eight hours later, the patient's condition was still more alarming, and because the presence of a clot on the opposite side was suspected, a right subtemporal decompression was performed. When the dura was incised, a large, thin-walled cyst containing dark, semifluid blood was evacuated. The underlying cortex was entirely normal. No fresh bleeding followed the evacuation, and the wound was closed without drainage. The patient made a complete uneventful recovery, and has remained well to date.

Summary.—In this case a man sustained a cranial trauma resulting in mild symptoms for four weeks, followed by a symptom-free interval of three weeks. Seven weeks after the trauma, he had a three-day period of amnesia, and one week later passed into stupor. An encysted subdural hematoma was found on the side opposite to that indicated by the symptoms. This history differs in but few details from that in many cases reported in the literature.

CHARACTER OF THE LESION

The gross as well as the microscopic characteristics of these lesions are of interest. Grossly, the outer wall of the hemorrhagic cyst, which is next to the dura, is a great deal thicker than the inner wall, which is next to the arachnoid. The outer wall is adherent to, but strips easily from, the inner surface of the dura, leaving relatively few bleeding points. As a rule, the inner wall is not at all adherent to the arachnoid and is avascular. The contents of the cysts vary from a thin yellow or brown fluid containing shaggy remnants of degenerating clot to a firm currant-jelly clot.

The microscopic appearance of the neomembrane surrounding the degenerating clot has been well described by many authors, notably by Putnam and Cushing [2] in 1925. Briefly, the outer wall may be said to resemble a highly vascular layer of granulation tissue of varying thickness, slightly adherent to the inner surface of the dura. Putnam and Cushing were particularly impressed with the frequent occurrence

2. Putnam, T. J., and Cushing, Harvey: Chronic Subdural Hematoma: Its Pathology, Its Relation to Pachymeningitis Hemorrhagica and Its Surgical Treatment, Arch. Surg. **11**:329 (Sept.) 1925.

of a layer of large irregular "mesothelial-lined blood spaces" in the neomembrane just below the line of demarcation between the dura and the membrane. The inner wall of the cyst is much thinner, and consists of a layer of fibrous tissue, a few cells in thickness, with a single layer of mesothelium on the surface next to the arachnoid. This portion of the membrane is entirely avascular.

In cases of subdural hematoma it is seldom possible to demonstrate the original source of the hemorrhage. The preponderance of evidence, however, would seem to indicate that the vascular rupture occurs in one or more of the cerebral veins as they cross the subdural space to enter the longitudinal sinus.[3] Certainly this is the most likely source of subdural hemorrhage during the course of a cranial operation.

THE LATENT INTERVAL

With this introduction, consideration may be given to the latent interval between the occurrence of the trauma and the onset of symptoms of increased intracranial pressure. In analyzing a large series of case reports of traumatic subdural hematoma, it is difficult to escape the conviction that the lesion must undergo a progressive augmentation in size subsequent to its initial formation. Otherwise, why should a patient, apparently completely recovered from the effects of a cranial trauma, begin to show symptoms of increasing intracranial pressure some weeks or months later?

The most obvious explanation of the progressive enlargement of these lesions is that there occurs a slow, continuous or perhaps an intermittent bleeding from the responsible vessel.[3] Yet, nowhere else in the body does an injured blood vessel behave in this fashion. These lesions occur in persons of any age; vascular disease does not constitute an etiologic factor, and a hemorrhagic diathesis has never been demonstrated.

It has been suggested[2] that the granulation tissue that constitutes the outer wall of the hematoma may be the seat of repeated hemorrhages, either from a capillary source or from the large "mesothelial-lined blood spaces," which appear to communicate with the capillaries. Arguments against this hypothesis are that spontaneous hemorrhage does not occur from newly formed blood vessels elsewhere in the body, and furthermore, the gross contents of a clinically progressive hematoma, as disclosed at operation or necropsy, are usually found to be perfectly homogeneous.

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3. Trotter, Wilfred: Chronic Subdural Hemorrhage of Traumatic Origin and Its Relation to Pachymeningitis Haemorrhagica Interna, Brit. J. Surg. **2**:271, 1914.

From the microscopic appearance of the membrane and from negative cultural studies of the contained fluid, it does not appear that infection can be responsible for a progressive enlargement of these lesions.

Taking all factors into consideration, it would appear that the peculiar behavior of these lesions must be the direct result of their environment. The subdural space has received surprisingly scant attention in the medical literature. Although the neurologic surgeon traverses this space almost daily, he rarely gives it much thought. Yet it is unique anatomically—a potential space lined with mesothelium, its outer wall constituted by the dura and its inner wall by the avascular arachnoid, with the cerebrospinal fluid space just beneath.[4] Curiously, nature has provided no obvious means of draining this space. The pericardial, pleural and peritoneal spaces all have their subserous systems of lymphatics to carry off débris. The presence of lymphatics, however, has never been demonstrated in the dura or in the arachnoid, unless one considers the subarachnoid spaces as lymphatic channels. This apparent lack of adequate lymphatic drainage from the mesothelial-lined subdural space, therefore, may provide the explanation for the curious progressive behavior of the subdural hematoma. Since the subdural space continues over the pacchionian bodies, as demonstrated by Winkelman and Fay,[5] it seems likely that elimination of subdural extravasations may occur at these points as well as along the nerve sheaths, provided that the extravasation is not too large.

EXPERIMENTAL STUDIES

In order to study the behavior of these lesions, attempts were made to reproduce them in animals, in spite of the failures of previous investigators.

In five dogs, a trephine opening was made over the parietal area, which was followed by a cisternal puncture to relax the unopened dura. With a fine curved hypodermic needle, from 0.7 to 3 cc. of whole, unclotted blood from the femoral vein was injected beneath the dura. A muscle graft was then placed over the puncture wound to seal it, the button of bone replaced and the wound closed. When the animals were killed, from three weeks to three and one-half months

4. Penfield, by an ingenious process, has demonstrated the presence of a small amount of yellow fluid in the subdural space of the dog (The Cranial Subdural Space, Anat. Rec. **28**:174, 1924), and he has also described a pathologic collection in the human being (Subdural Effusion and Internal Hydrocephalus, Am. J. Dis. Child. **26**:383 [Oct.] 1923).

5. Winkelman, N. W., and Fay, T.: Pacchionian System: Histologic and Pathologic Changes with Particular Reference to Idiopathic and Symptomatic Convulsive States, Tr. Am. Neurol. A. **55**:274, 1929.

later, there was little or no gross evidence of the injected blood beneath the dura. This has also been the experience of previous investigators in this field.[6]

That an overlying cranial defect might in some way favor the regression of a subdural hematoma was suggested by the fact that a progressive type of lesion never follows a cranial operation. Therefore, in order to avoid the presence of a cranial defect directly over the experimental lesion, the following procedure was carried out on seven dogs.

A small drill hole was made in the parietal region and was followed by a cisternal puncture with the removal of from 5 to 10 cc. of fluid. A curved lumbar puncture needle was then passed through the brain across the midline until the point came to rest beneath the intact cranial vault on the side opposite to the drill

Fig. 2.—Method of transcerebral injection of blood into the subdural space.

hole. At this point from 3 to 11.5 cc. of whole, unclotted blood from the femoral vein was injected (fig. 2). Again, at autopsy little gross evidence of the injected blood was found if more than a couple of weeks had elapsed since its introduction.

COMMENT

In this series of experiments large dogs, weighing from 45 to 60 pounds (20.4 to 27.2 Kg.), were used in order that larger amounts of blood might be injected. The animal into which 11.5 cc. was injected died within a few hours after the experiment had been performed. At necropsy, the blood was found to be generally distributed over the hemisphere, but at no point was the clot more than 1.5 mm. in thickness. This suggested that the failure to reproduce the progressive

6. Footnote 4, first reference.

clinical lesion might be due to failure to obtain a sufficiently thick layer of injected blood in the experimental animal.

Attention was then diverted temporarily to a study of the comparative osmotic pressures of the blood and spinal fluid.

Semipermeable collodion membranes were first used, but were soon discarded on account of their fragility. Cellophane proved to be much more adaptable. This membrane was found to be permeable to the molecules of salts and dextrose of whole blood but not to the larger molecules of protein. In experiments in vitro it was found that when whole blood was separated from cerebrospinal fluid by a membrane of cellophane, no. 300, there was an osmotic imbalance of about 20 mm. of

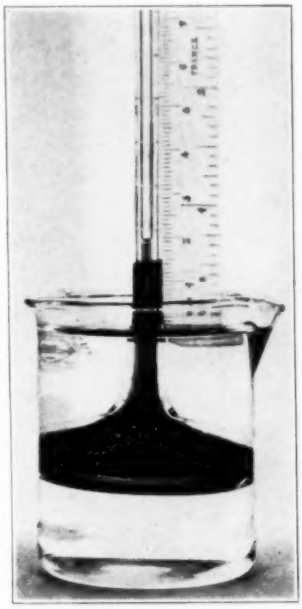

Fig. 3.—Method of demonstrating the osmotic imbalance of the protein in the blood and spinal fluid. The beaker contains the spinal fluid, and the inverted funnel is closed with a tambour of cellophane containing the blood.

water in favor of the blood (fig. 3). It was therefore assumed that 20 mm. of water represented the fractional osmotic pressure of the proteins of the blood against that of the proteins of the spinal fluid.

Further tests were then made. With aseptic precautions, two cellophane sacs containing whole blood taken from a patient on a fasting stomach were dialyzed against the patient's spinal fluid (fig. 4). One test was carried out in the refrigerator at 0 C. and one in the incubator at 37 C. Each day, the sacs were removed from the fluid and weighed aseptically. The initial weight of the sac that was kept at 0 C. was 1.864 Gm. In eighteen hours, it had increased 37.1 per cent of its original weight; in forty-four hours, 57 per cent, and in sixty-six hours, 73.5 per cent. The initial weight of the sac that was kept at 37 C. was 1.286 Gm. In eighteen hours, it had increased 59 per cent of its original weight; in forty-four hours, 78.2 per cent, and in sixty-six hours, 93 per cent.

In a series of eight dogs, cellophane sacs, of known weight, containing whole blood from the femoral vein were inserted in the subdural space. The sacs with their contents were removed later and weighed in order to note any increase in weight. In five of the animals similar sacs were also placed in the rectus sheath or peritoneal cavity. In one animal, which was killed after fifty-one days, both sacs were found to be ruptured. In the remaining animals the sacs were intact when removed from three to eighteen days after implantation. After removal each sac was found to have gained from 39 to 103 per cent in weight. With one exception, the control sacs in the rectus sheath and peritoneal cavity gained more in weight than did the sacs in the subdural space.

Tests with Living Neomembrane.—An opportunity of testing the permeability of the living neomembrane then presented itself. A portion of an inner cyst wall was removed from a patient at operation, two and one-half months after a cranial trauma.

Fig. 4.—Cellophane sac containing whole blood immersed in spinal fluid for the purpose of observing the increase in weight of the sac.

Seventeen cubic centimeters of the fluid contents of the hemorrhagic cyst was dialyzed against 52 cc. of the patient's spinal fluid, the cyst wall being used as the dialyzing membrane. This preparation was made under aseptic precautions and placed in the refrigerator for sixteen hours. At the end of this time the hemorrhagic fluid had increased 2.9 per cent in volume after it had returned to room temperature. The total protein [7] of the surrounding spinal fluid, estimated by the Kjeldahl method, was the same after the experiment as it had been before.

7. The protein content of the cyst fluid was 8.2921 per cent. The protein content of the spinal fluid was 0.854 per cent before and 0.8406 per cent after dialysis. This slight difference is within the limits of experimental error. The measurements were made by Dr. John W. Shirer.

COMMENT

The measurements indicate that the neomembrane is permeable to fluid but not to protein molecules, and that an osmotic imbalance exists which is in favor of the cyst contents.

In the light of the experiments cited, the latent interval in cases of subdural hematoma may be explained as follows:

Following a cranial trauma, hemorrhage occurs into the subdural space, probably from a rupture of one of the cerebral veins where it crosses the space to enter the sagittal sinus. A large amount of blood, having escaped, becomes clotted, and within the course of a few days this clot is surrounded by a capsule of mesothelium and connective tissue growing out from the dura. That this capsule forms with remarkable rapidity is attested by clinical as well as by experimental observations.[8] The portion of the capsule next to the dura becomes invaded with nutrient capillaries from the dura and thus attains a greater thickness than does the avascular portion that is adjacent to the avascular arachnoid. The encapsulated clot then undergoes partial liquefaction, with a resultant fluid high in protein content. This fluid is separated from the cerebrospinal fluid, which is of low protein content, merely by the thickness of a few layers of cells constituting the inner wall of the cyst and the arachnoid membrane. There then results an ideal set-up for osmotic interchange. Since the neomembrane is impermeable to the large protein molecules in the hemorrhagic fluid, an osmotic imbalance in favor of the hemorrhagic fluid must exist, resulting in the withdrawal of cerebrospinal fluid into the cyst. This, of course, causes a progressive enlargement of the hemorrhagic cyst and eventually a rise in intracranial pressure.

CONCLUSIONS

1. In cases of subdural hematoma there occurs a gradual increase in the size of the lesion following its initial formation.

2. The progressive behavior of these lesions is due to their environmental conditions, particularly to the inadequacy of lymphatic drainage from the mesothelial-lined subdural space.

3. The actual increase in size of the subdural hematoma is due to an accession of tissue fluid, particularly spinal fluid.

4. This fluid is drawn into the hemorrhagic cyst through the semipermeable arachnoid membrane and adjacent cyst wall by the osmotic tension of the blood proteins contained in the cyst.

5. It is difficult, if not impossible, to reproduce in the dog the clinical picture of subdural hematoma.

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8. Putnam, T. J., and Putnam, I. K.: The Experimental Study of Pachymeningitis Haemorrhagica, J. Nerv. & Ment. Dis. **65**:260, 1927.

ABSTRACT OF DISCUSSION

Dr. Francis C. Grant, Philadelphia: Dr. Gardner has afforded us a logical outline of the way in which a chronic subdural hemorrhage forms and a satisfactory explanation of the latent interval that commonly precedes the appearance of symptoms in cases of this type.

From a study of the pathologic process observed in this particular condition, it is certain that in the beginning, at least, the clot is solid; that the blood supply of the clot extends into it from the surface in contact with the dura, and that the membrane over the clot on the arachnoid side is relatively thin and avascular. Consequently, the interior of the clot is not well supplied with blood, and liquefaction necrosis occurs in its center producing precisely the picture that has been described, namely, a sac filled with this curious coffee-colored material, high in protein.

That the high protein content of this fluid can attract cerebrospinal fluid by osmosis through the thin sac wall lying against the arachnoid fluid spaces is strongly suggested from the evidence of the experiments that Dr. Gardner has carried out.

From the clinical standpoint the development of symptoms in these cases fits in well with the theory he has proposed. An injury is sustained from which recovery is often complete. Then occurs the latent interval, which may be very long, and during which symptoms may not appear. The slow development of evidence of intracranial involvement follows, at times sudden in its onset, and then occurs the abrupt appearance of overwhelming symptoms that promptly turn the attention of those in charge to the fact that there is a serious intracranial complication. This sequence of events certainly suggests a slowly enlarging lesion, difficult at times to differentiate from tumor of the brain, and this fits in extremely well with the theory propounded. As this sac slowly fills up and expands, the brain adjusts itself to the increase in size of the fluid mass, and when further adjustment becomes impossible an overwhelming development of symptoms occurs that may place the patient in a critical condition.

So far as clinical experience is concerned, there is nothing that does not accord satisfactorily with Dr. Gardner's theory.

Dr. Tracy Putnam, Boston: There are three factors in the pathology of these interesting lesions that have been difficult to explain. The first one is the source of the blood which often appears as a result of a trifling trauma, as Dr. Gardner has pointed out.

Recently I have been fortunate enough to see a specimen in Dr. Timothy Leary's laboratory in which a subdural hematoma occurred about twenty-four hours after a rather mild trauma. An aberrant vein was demonstrated, and I believe that that is probably the explanation of the origin of the bleeding.

Dr. Gardner's demonstration of the increase in the volume of blood within a dialyzing sac agrees with an explanation made on purely *a priori* grounds by Dr. Frank Fremont-Smith, in a case of ours. He pointed out that an encysted hematoma must break down, with the formation of much smaller molecules. The molecular weight of the protein of the blood is several thousand, and these must break into molecules perhaps not larger than several hundred, with a manifold increase in osmotic pressure.

This seems a more reasonable explanation than that the blood itself is inherently hypertonic to the spinal fluid, which we know is not the case; normally the osmotic pressure of the two is almost exactly the same, as was shown by Mestrezat and others.

The third puzzling factor in the pathology of this disease is the enormous size of the capillaries. I have not the slightest notion why this is so. I wish that some one would explain it.

Dr. William G. Spiller, Philadelphia: I have seen a considerable number of such cases over a long period of years. The latent period is perhaps the chief diagnostic factor. In a case of trauma of the skull with a latent period followed by the development of focal symptoms, one may reasonably make a diagnosis of a probable subdural hemorrhage and advise operation.

It is amazing to what extent such hematomas may increase in size. In two instances I have seen an entire cerebral hemisphere flattened by an enormous subdural hematoma, and I have even seen a hematoma covering both cerebral hemispheres, and the patient has lived with this intracranial pressure.

About thirty years ago Dr. McCarthy and I attempted to determine the method by which the hematoma forms, following the views of Virchow, but no thoroughly satisfactory explanation has been offered. Dr. Gardner presents what seems to be a reasonable theory.

Dr. J. Jay Keegan, Omaha: I should like to report a case that confirms Dr. Gardner's statement that the origin of a subdural hematoma is from torn veins that cross from the cerebral cortex to the superior sagittal sinus.

In my patient left parietal lobe symptoms developed two months after a slight frontal injury. A subdural hematoma was suspected. A trephine opening was made in the left parietal region, and a large quantity of dark liquid blood was drained out of the subdural space. The entire hemisphere appeared markedly compressed.

After complete evacuation of the old blood and irrigation of the cavity with a saline solution, an intermittent bleeding point was seen far forward, apparently coming from an opening in the anterior portion of the superior sagittal sinus. This bled only when the patient moved or strained. A piece of temporal muscle was placed over the opening, and no further bleeding occurred during closure. A drain was left in the cavity.

Recurrent signs of hemorrhage and pressure developed shortly after the operation, and a left frontal trephine opening was made to expose the bleeding point better. The bleeding definitely came from the superior sagittal sinus. The opening was closed with silver clips and coagulation, but the patient died of an acute cerebral edema resulting from the pressure disturbance in the left hemisphere.

Dr. Samuel Brock, New York: In Dr. Foster Kennedy's neurologic service in Bellevue Hospital, New York, nine cases of subdural hematoma were studied recently by Dr. A. Kaplan. Dr. Gardner mentioned the matter of false localizing phenomena in passing. To me it is a very practical point.

In five of these nine cases the hemiplegia was present on the same side. This peculiarity has been noted by other clinicians. It is such a frequent occurrence that in a suspected case, a trephine opening should be made on the homolateral side if a plum-colored subdural hematoma is not found when the dura on the side contralateral to the hemiplegia is opened. Whether the homolateral hemiplegia is due to the pressure exerted by the opposite hemisphere, the brain being pushed over by the soft mass (a contrecoup effect), or whether it is due to a mechanism recently described by Kernohan and Woltman, in which the opposite crus is cut by the sharp free edge of the tentorium consequent on downward pressure, are open questions. One wonders why such false localizing signs do not occur more often in tumors of the brain. Perhaps Dr. Gardner can throw light on this phase of the subject, as well as on the matter of pathogenesis.

Dr. W. James Gardner, Cleveland: In reply to Dr. Putnam, it is, of course, a well established fact that the total osmotic pressure of the blood and cerebrospinal fluid, as determined by the freezing point method, are identical, but if these two fluids are separated by a semipermeable membrane that holds back the protein molecules, an osmotic imbalance exists which represents the difference in protein concentration of the two fluids. Undoubtedly, in cases of traumatic subdural hematoma, as the encysted clot liquefies the protein molecules begin to split up, with the result that as the age of the hematoma increases there are many times more protein molecules than there were originally, with the consequent increase in the osmotic tension of the trapped fluid.

There are several factors concerning hematomas that lack explanation. In a recent case in which we exposed the hematoma at operation, a Wassermann needle was introduced through the dura before any attempt at incision was made, and a large quantity of dark hemorrhagic fluid was removed. Microscopically, a smear of this fluid was indistinguishable at first glance from a smear of fresh blood, although the lesion was certainly two and a half months old. The red cells were well formed, perhaps a little smaller than normal; there was little change in their shape; the interesting thing, however, is that there was no fibrin present, and practically all of the white cells present were eosinophils. Those facts are a little difficult to explain.

In answer to Dr. Brock's question as to why there are homolateral signs, it seems to me that the explanation is that which he suggests. The homolateral signs which so frequently occur are due to a dislocation of the brain and the brain stem to the opposite side, with consequent encroachment of the incisura of the tentorium on the contralateral crus.

The absence of localizing signs in the cortex immediately beneath the hemorrhage is readily explained because of the fluid consistency of the lesion. The arachnoid is intact, and there is apparently no damage to the cortex underlying it.

AMYOTROPHIC LATERAL SCLEROSIS WITH MENTAL SYMPTOMS

A CLINICOPATHOLOGIC STUDY *

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Amyotrophic lateral sclerosis is generally regarded as a disease limited to involvement of the motor system, mainly the pyramidal tracts, the bulbar nuclei and the anterior horn cells. Degeneration of the upper motor neuron begins in the giant pyramidal cells of Betz and extends throughout the neuraxis. The occurrence of mental symptoms was not mentioned by Charcot, but subsequent observers called attention to their existence in isolated cases. The question has always arisen whether the psychotic manifestations were part of the syndrome of amyotrophic lateral sclerosis and could be attributed to the same degenerative process or were the result of cerebral changes which by chance happened to be associated with the upper and lower motor neuron disease. While the cases we shall report do not entirely answer the question, the three that came to necropsy, we believe, throw some light on the problem.

REPORT OF CASES

CASE 1.—*History.*—H. L., a man, aged 38, married, a fruit pedler, who was admitted to the Montefiore Hospital on Jan. 2, 1930, in November, 1927, had begun to show mental changes characterized essentially by impairment of memory. The family noticed that he was "tongue-tied," reiterated statements without being aware of what he said, could not recall the names of his parents and failed to recognize the members of his family or the house and street in which he lived. He was unkempt, unconcerned, somewhat hesitant and stammering.

In June, 1928, the patient was seen by a neurologist, who found atrophy of the arms and hands. At Mount Sinai Hospital, where he was from Oct. 5 to 28, 1928, a diagnosis of amyotrophic lateral sclerosis was made. He gradually became worse: his face became expressionless, he grew more careless about his person, at times he went without clothes, and he urinated any place about the house. He lost interest in his surroundings and was unable to pay any sustained attention. In December,

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1929, he left his house and was found at one of the city hospitals; he had abrasions of the forehead and face. Except for an old neisserian infection, the past and family histories were without significance. He had three children, all of whom were left-handed.

General Examination.—There were several scars from abrasions in the right malar region, on the right forearm and on the left mentum, which were apparently traumatic and appeared to be a few weeks' old. The heart was slightly enlarged. There were slight signs of arrhythmia. The peripheral vessels showed moderate thickening of their walls.

Neurologic Examination.—The patient was fairly well developed. He held his head rigidly. His face had an expressionless stare, and when he was amused it showed a sort of idiotic smile. Speech was limited to monosyllables; he tended to perseverate and answered "yes" repeatedly. He had difficulty in unbuttoning his coat or removing his clothes owing to motor weakness. Motor power was diminished in the upper extremities, more so on the right, and to a lesser extent in the lower extremities. On extension of the arms there was a fine tremor of both hands, which was more marked in the right thumb and index fingers. There was an occasional tremor of the left lower extremity. Fibrillations were most marked in the neck and shoulder muscles, the left platysma, sternocleidomastoids, pectorals and deltoids. In addition, there were irregular, coarse, muscle fiber contractions in the thigh and calf muscles and around the axillae. There was a right wrist-drop. The tongue showed marked atrophy and fibrillation. There was atrophy of the muscles of both upper extremities, most pronounced in the supraspinatus and infraspinatus, the right deltoid, the muscles of the forearm and the thenar and hypothenar eminences. The jaw and pectoral reflexes were present. The knee and ankle jerks were hyperactive. There was no Babinski sign. The sensory status could not be determined, but the patient appeared to feel pinpricks all over equally well. The optic disks were hazy and slightly irregular in outline. There was a slight internal strabismus and ptosis of the right lid. The pupils were round and equal, but slightly irregular; they reacted sluggishly to light and better in accommodation and on convergence. There was flattening of the right nasolabial fold. The right side of the face did not move as well as the left, either voluntarily or on emotional innervation. The tongue protruded to the right; it was rigid and furrowed. The palate moved equally well on both sides.

The muscles of the upper extremities showed a quantitative diminution of response to the faradic current. On galvanic stimulation the flexors of the forearm and hand showed almost equal cathodal and anodal closing contraction. In general, the muscular contractions were delayed and slowed.

Mental Examination.—The patient was neglectful of his personal appearance. He knew his name, and repeated it three or four times at irregular intervals when asked for it. He was congenial but not capable of cooperating. He appeared slightly interested in his surroundings as long as there were variations, but this interest soon waned. He would answer questions occasionally with either "yes" or his name. He was disoriented for place and person. He wandered aimlessly about the ward, smiled fatuously and reacted to no particular situations. At times he obeyed simple commands correctly, but failed to accomplish any complicated acts. Owing to his inaccessibility, an accurate study of the mental content and intellectual capacity could not be made. The inability to express himself was more than a dysarthria and partook of some degree of asphasia in addition to a profound intellectual deterioration. His affective responses were inappropriate. The mental picture resembled in the main an advanced dementia.

Laboratory Data.—On Feb. 1, 1930, a roentgen examination of the chest showed a partial consolidation of the lower lobe of the right lung, which gave the appearance of a resolving pneumonic process. The other lobes were normal. Chemical analysis of the blood showed: sugar, 82 mg.; urea, nitrogen, 32 mg. The blood pressure was 138 systolic and 100 diastolic. Manometric tests of the spinal fluid gave normal results; there were: a marked trace of albumin, 100 lymphocytic cells and a total protein of 34 mg. per hundred cubic centimeters. The Wassermann reaction was negative. Examination of the blood showed 10,200 white cells and 4,100,000 red cells, with a normal differential count.

Course.—The patient became more markedly deteriorated mentally and aphasic. Bronchopneumonia developed, and he died on Jan. 30, 1930.

Autopsy.—Gross Examination: Brain: There were congestion of the cerebral vessels and atrophy of the frontal convolutions with a wide separation of the fissures of the frontal lobes. The left centrum ovale was firm to palpation, shrunken and showed a mild lacunar state. The gray matter appeared atrophic. The diencephalic and mesencephalic structures showed an unusual amount of pigmentation. The lateral ventricles were enlarged, more so on the left, with a marked dilatation of the third ventricle. In the pontile region, the aqueduct showed thickening of the ependyma and choroid with obstruction of its channel.

Spinal cord: The dura showed a slight accumulation of blood in the vicinity of the roots of the lower dorsal and lumbar regions, more so on the left. The spinal cord was cut at various levels, and translucency of the crossed pyramidal tracts, greater on the left, was found.

Microscopic Examination: Frozen and celloidin sections of the brain from various regions were stained by the myelin sheath stain (Weil modification), Mallory's phosphotungstic acid stain, hematoxylin and eosin, cresyl violet, sudan IV and by the Cajal gold sublimate (Globus' modification), Bielschowsky, del Rio Hortega (Penfield modification) and Victoria blue methods.

Cerebral Hemispheres: Frontal region: In the region of F_1, F_2 and F_3, the meninges were slightly thickened; this was most marked over the right F_1. The cortical layers of F_1, F_2 and F_3 were narrower than normal. The nerve cells of the various layers showed poor Nissl substance, satellitosis, occasional neuronophagia and ischemia. There was scantiness of the ganglion cells, with a disturbance in the architectural arrangement of the layers of the cortex, the process being more marked in the fifth and sixth layers (fig. 1 *A*). Very small areas of destruction (Verödungsherde) were found in the cortical layers. These had an increase in the number of glia cells, as well as a slight swelling of the oligodendroglia. A marked area of rarefaction was found in the left second frontal convolution. The white matter of both frontal areas, especially on the left, showed an increase in the astrocytes, the fibrillary type predominating. Perivascular infiltration, consisting primarily of cells of glial origin, was also observed in the centrum ovale. The axis cylinders stained poorly with the Bielschowsky stain, and some were completely broken down.

Precentral, postcentral, parietal and temporal areas: The same changes were observed as in the frontal region (fig. 1 *B*), except that the second and third cortical layers on the left side were somewhat destroyed and contained an increase in the microglia and swollen oligodendroglia cells. Verödungsherde were also found. The giant Betz cells of the precentral area were markedly diminished in number and showed a lack of Nissl substance, satellitosis and neuronophagia. A few normal giant pyramidal cells were seen. The same process was observed in the temporal and part of the parietal areas. There was some meningeal infiltration. In

the right temporal region and near the hippocampus a few of the vessels showed definite arteriosclerotic changes, manifested primarily by thickening of the adventitial coat, which was free from any perivascular infiltration. Occasional vessels with perivascular infiltration were found in the white matter of the temporal and parietal lobes. This entire process was more marked on the left.

The region of the diencephalic structures: Sections showed dilatation of the anterior horns of the lateral ventricles, more so on the left, a dilated third ventricle and a markedly shrunken white matter of the left side. The ependymal lining

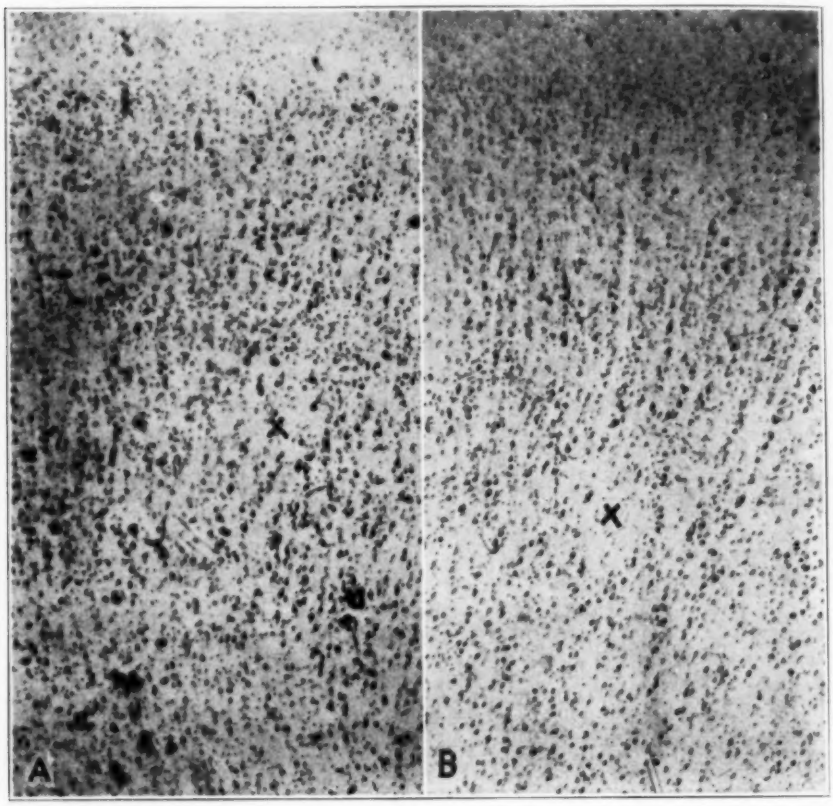

Fig. 1.—Left frontal area (*A*) and right motor area (*B*), showing disturbances in the architectural arrangement of the cortical layers, falling out of the nerve cells and areas of destruction (*x*). Cresyl violet stain; × 40.

throughout was thickened, and in places warty excrescences were observed. On the right side, above the caudate, the ependymal lining showed a subependymal reaction consisting of swollen oligodendroglia and microglia cells. The right internal capsule showed an area of marked perivascular infiltration consisting of compound granular corpuscles and glia cells. With the sudan IV stain there was an accumulation of fat and a few round cells in one vessel. With the Bielschowsky stain the axis cylinders were seen to be partially destroyed. The vessels of the meninges near the hippocampus showed thickened adventitia. The right internal

capsule remained unaffected. Some of the nerve cells of the thalamus, caudate nucleus, putamen and globus pallidus showed slight changes, chiefly in the form of satellitosis. An occasional nerve cell undergoing neuronophagia was also observed. There were marked destructive changes in the nerve cells of the paraventricular nuclei, such as poor Nissl substance, complete loss in the outline of the cell and neuronophagia.

The midbrain: Sections did not show any involvement, the red nucleus, substantia nigra, etc., all being spared. A few of the pontile motor cells showed satellitosis, poor Nissl substance and occasional neuronophagia. The pyramidal tract fibers took a slightly paler stain than normal. The nerve cells of the motor nucleus of the fifth nerve showed very slight changes. Sections in the region of the tenth and twelfth nerve nuclei showed paling of both pyramids and definite thickening of the ependymal lining of the fourth ventricle with warty excrescences.

Fig. 2.—Transverse section from the midthoracic region, showing demyelinization of the crossed and direct pyramidal tracts as well as the dorsocerebellar pathways. Myelin sheath stain (Weil modification); × 30.

The nerve cells of the hypoglossal nucleus were scanty, and those remaining showed changes similar to those in the giant pyramidal cells of Betz in the motor cortex. The same changes, but to a less marked extent, were also observed in the nerve cells of the nucleus ambiguus. These two nuclei were the site of an increase in the glial elements. The anterior spinal vessel of the medulla oblongata showed slight perivascular infiltration.

Spinal Cord: Longitudinal and transverse sections were stained by the same methods as the brain.

Cervical region: With the myelin sheath stain there was complete demyelinization of the pyramidal tracts. With a higher power, the myelin sheaths were seen to be swollen and in places slightly disintegrated. With the Mallory phosphotungstic stain some of the smaller vessels showed endarteritic changes, especially in the anterior fissure. With the Victoria blue method the longitudinal sections

showed a slight gliosis, disorderly in fashion. With the sudan IV stain, a slight mass of fat was found in one area of the crossed pyramidal tracts. In Bielschowsky preparations, swollen and broken down axis cylinders, patchy in nature in the crossed pyramidal tracts, were seen. Normal axis cylinders were found adjacent to the destroyed ones. In hematoxylin and eosin sections, hemorrhages were observed in the gray matter, more so on the right (fig. 3), little in the involved fiber tracts and still less in the posterior columns. The central canal was widely open, but the ependyma was not thickened. The meninges were slightly thickened, but there were no evidences of inflammation. The anterior horn cells, especially in the left ventral region, were diminished (fig. 4); some were pyknotic and

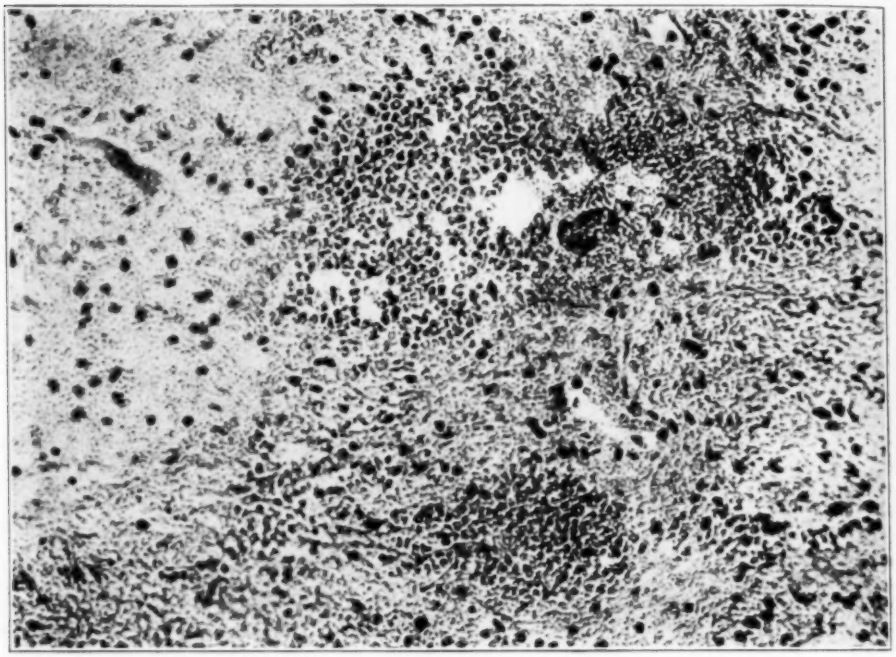

Fig. 3.—Multiple hemorrhages in the gray matter of the cervical cord; × 240. Hematoxylin-eosin stain.

others showed various changes, such as poor Nissl substance, ischemia, shrinkage, neuronophagia and complete destruction. The gray matter showed an increase in the glia cells, which belonged to the protoplasmic astrocytic group.

Thoracic region: Sections showed demyelinization of the crossed and direct pyramidal tracts, with less involvement of the right side (fig. 2). The hemorrhages observed in the cervical region were not found in this segment. The central canal was open throughout the thoracic portion of the cord. The anterior horn cells were better preserved than those in the cervical region, and only rarely were abnormal ones found. There were a few patchy areas of necrosis, best seen in Mallory phosphotungstic acid sections, near the vessels in the crossed pyramidal tracts.

Lumbar enlargement: Only the crossed pyramidal tracts were demyelinated, although with a higher power some changes in the myelin sheaths were also found in the direct pyramidal tracks. The central canal was open. The anterior horn cells were fewer in number than in the thoracic region, but most of them were fairly normal. Slight changes, such as a lack of Nissl substance and satellitosis, were found in these cells. One small hemorrhage was found in the direct pyramidal tract of the lumbar enlargement.

Sacral region: The anterior horn cells showed satellitosis and occasional neuronophagia. The central canal remained open.

Comment.—Clinically, in case 1 there were two syndromes: (1) nuclear involvement, mainly of the bulb and upper part of the spinal

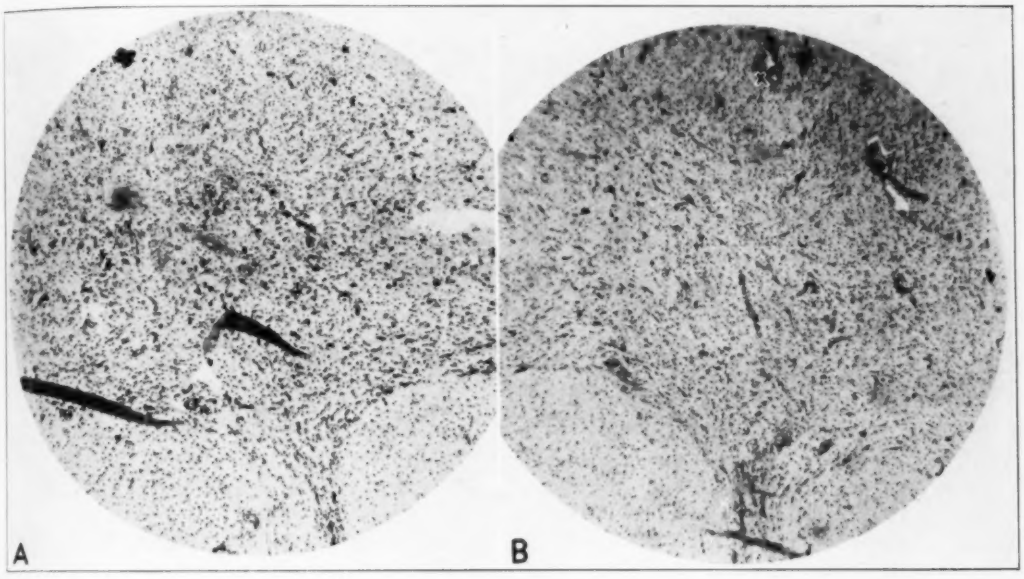

Fig. 4.—*A*, right gray matter of the cervical region, showing an increase in the glia nuclei. *B*, left gray matter of the cervical region, showing scantiness of the anterior horn cells, increase in glia nuclei (compare with *A*) and hemorrhages at *x*. Cresyl violet stain; reduced from a magnification of × 36.

cord, and pyramidal tract disease; these constitute the syndrome of amyotrophic lateral sclerosis; (2) a cerebral degenerative process characterized by mental deterioration (childishness, stubbornness, lack of cooperation, emotional instability and a tendency to euphoria and aphasia). The mental picture somewhat resembled Alzheimer's disease, though there was little to substantiate this, and certainly the anterior horn cell syndrome is foreign to it.

Histopathologically, the changes in the cortex, illustrated by the disturbances in the architecture of the cortical layers, extending from the

frontal to the temporal regions, scantiness of the ganglion cells with more marked changes in the fifth and sixth layers, Verödungsherde, perivascular infiltration in the white matter and slightly thickened meninges speak in favor of a degenerative process. These changes existed in addition to the ordinary process of amyotrophic lateral sclerosis seen in the giant pyramidal cells of Betz. In this case the disease had lost its selective character. It may, therefore, be considered as a chronic degenerative syndrome with a tendency toward sclerosis. The presence of reparative glial changes in close relationship with the degenerative process warrants the conclusion that the glial proliferation was primary. The thickening of the ependyma in the lateral, third and fourth ventricles also points toward a chronic process. The fairly uniform generalized internal hydrocephalus was the direct result of the obstruction of the aqueduct by the thickened ependyma. The picture simulated to some extent that seen in pseudosclerosis. While the changes in the crossed and direct pyramidal tracts and anterior horn cells were typical of amyotrophic lateral sclerosis, the hemorrhages seen in the cervical region are foreign to this disease, and as far as we know have never been described before. The opening of the central canal throughout the spinal cord is also noteworthy, for in the adult, except in the lumbar region, the canal is usually closed. The almost negligible pathologic changes in the gray matter of the thoracic region are also unusual.

Case 2.—*History.*—J. R., a man, aged 32, who was admitted to the Montefiore Hospital on May 30, 1930, in December, 1927, had begun to show weakness and unsteadiness of the left lower extremity. The condition had remained stationary until April, 1929, when, following a sore throat, difficulty in speech and weakness of the upper extremities developed. He was admitted to another hospital on Nov. 14, 1929, when he was found to have gluteal atrophy, exaggeration of all deep reflexes, more so on the left, a Babinski sign on the left, left facial weakness, deviation of the tongue to the left, marked dysarthria, dysmetria of the left upper extremity, spastic ataxia of the left leg and a slowness and slurring of speech. Multiple sclerosis was considered as a diagnostic possibility. The family and past histories were without significance.

General Examination.—The results were negative.

Neurologic Examination.—The patient was bedridden and presented a picture of progressive lenticular degeneration, as shown by rigidity, drooling, spasmodic laughing and crying, and mental deterioration. There was unsteadiness in the upper limbs. The speech was dysarthric, explosive, scanning and at times monotonous. The interossei were atrophied, and there were generalized fibrillary twitchings, massive in character, of the arm, forearm, hand, leg and shoulder girdle muscles. There was increased tonus in all limbs. The left foot had a striatal attitude, and cogwheel phenomena were present in the upper extremities. Power was diminished in all extremities, more on the right side. There was generalized

hyperreflexia with a positive Babinski sign and absent abdominal reflexes. The fundi were normal. The right corner of the mouth drooped. Emotional innervation was good. The tongue deviated to the left. There was frequent spasmodic laughter and crying. Mentally, the patient was retarded and apathetic, and he cooperated poorly. Memory was poor for recent and remote events. The patient was disoriented. When asked why he laughed or cried, he said, "I can't help it," but when told to do so he stated, "I cannot do it."

Course.—Difficulty in swallowing and breathing began to develop. At no time were there noticed any fibrillations or atrophies of the tongue. On Nov. 7, 1930,

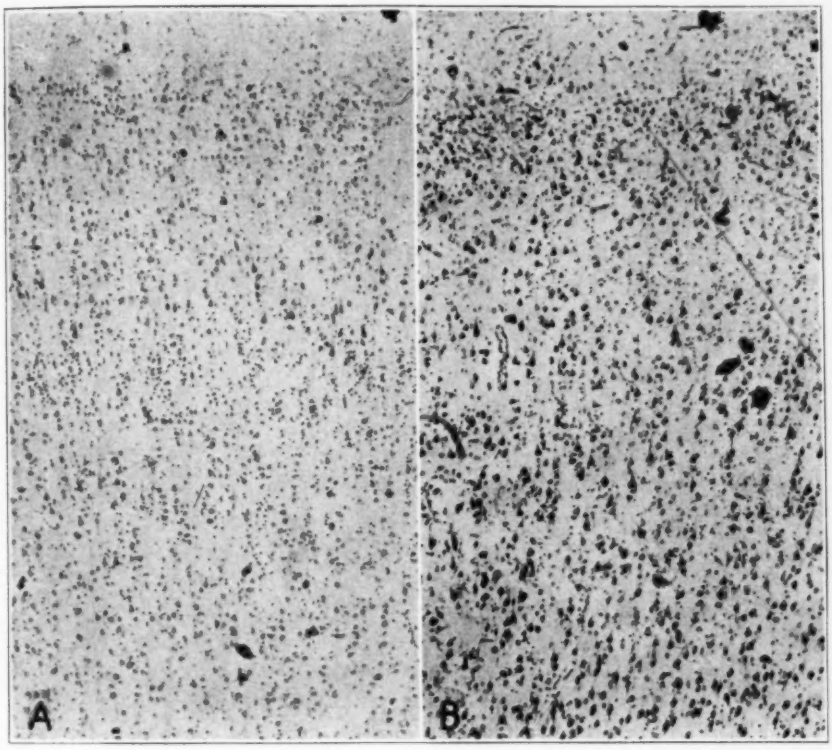

Fig. 5.—*A*, frontal area, showing well preserved cytoarchitectural layers and scanty and poorly stained ganglion cells of the third, fifth and sixth layers. *B*, motor area, showing disturbance in the architectural arrangement of the cortical layers, with destruction of some of the ganglion cells. Cresyl violet stain; × 40.

fever developed and the patient became cyanotic; he died as a result of aspiration pneumonia on November 8.

Laboratory Data.—The blood pressure was 135 systolic and 90 diastolic. A roentgenogram of the skull showed a faint streak of calcification above and to the right of the pineal gland. The possibility of a neoplasm was considered. The results of all other laboratory tests were negative.

Clinical Diagnosis.—The diagnosis was amyotrophic lateral sclerosis and progressive lenticular degeneration, possibly caused by encephalitis.

Autopsy.—Gross Examination: Brain: All blood vessels were markedly congested. The convolutions from the frontal to the postcentral regions were atrophic and the fissures were widely separated. The brain was cut coronally. The cortical gray matter appeared narrower than normal. The white matter of the right corona radiata, in the region of the caudate and putamen, was shrunken.

Spinal cord: This appeared anemic. On section there was a translucency of the crossed pyramidal tracts. The gray matter was slightly hemorrhagic.

Frozen and celloidin sections of the entire nervous system were stained by the methods used in the previous case.

Microscopic Examination: Frontal lobes: The pia-arachnoid showed thickening in places, consisting of proliferated arachnoidal cells, and the vessels showed

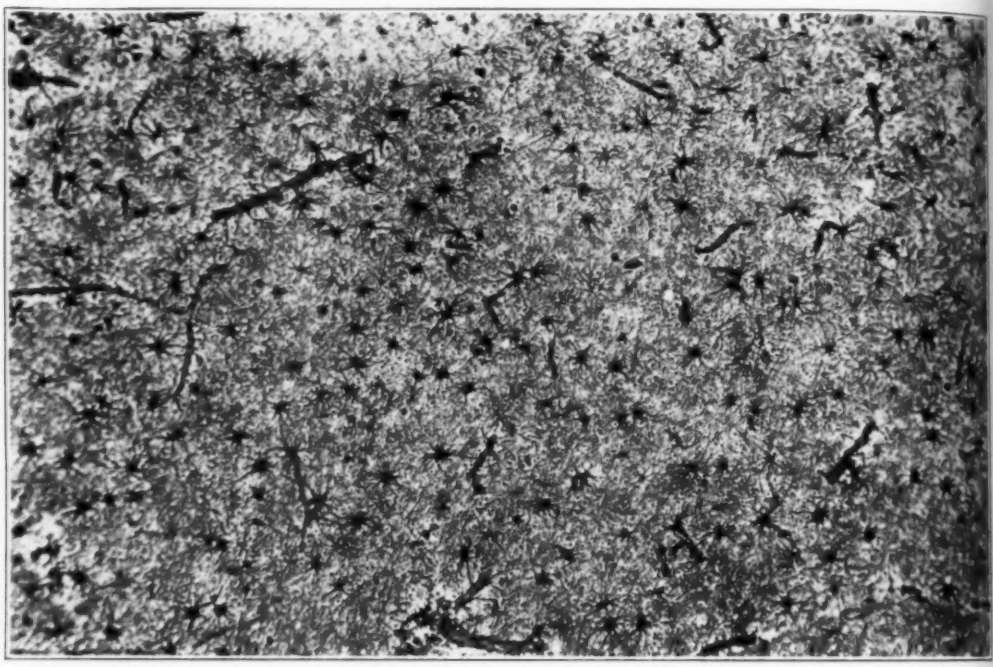

Fig. 6.—Increase in the fibrillary astrocytes of the white matter of the cortex. Cajal gold sublimate method (Globus modification); × 100.

moderate atherosclerotic changes. The architectural arrangement of the cortical layers was fairly well preserved. The ganglion cells of the third, fifth and sixth layers were fewer in number, stained poorly, had little Nissl substance and showed pathologic changes in acute and chronic stages (fig. 5*A*); the cells of the fifth layer were more involved than those in the other two layers. The nerve cells in this area were completely disintegrated and showed marked chromatolytic changes. Definite foci of destruction (Verödungsherde) were found in the vicinity of occluded and proliferated vessels. The capillaries in the superficial zones were increased and showed distinct intimal proliferation; some were completely occluded. The white matter, particularly on the right side, stained poorly but did not show any evidence of breaking down of the myelin sheaths. In Cajal's gold sublimate sections, this area was filled with numerous protoplasmic and fibrillary astrocytes

(fig. 6). The third, fifth and sixth cortical layers showed an increase in the protoplasmic astrocytes and microglia cells.

Precentral gyrus: The same changes were observed as in the frontal gyri, except that the cortical laminae had lost their normal architectural arrangement (fig. 5*B*). The giant pyramidal cells of Betz were also affected. The white matter was filled with proliferated and occluded small vessels, some of which showed evidence of beginning calcification.

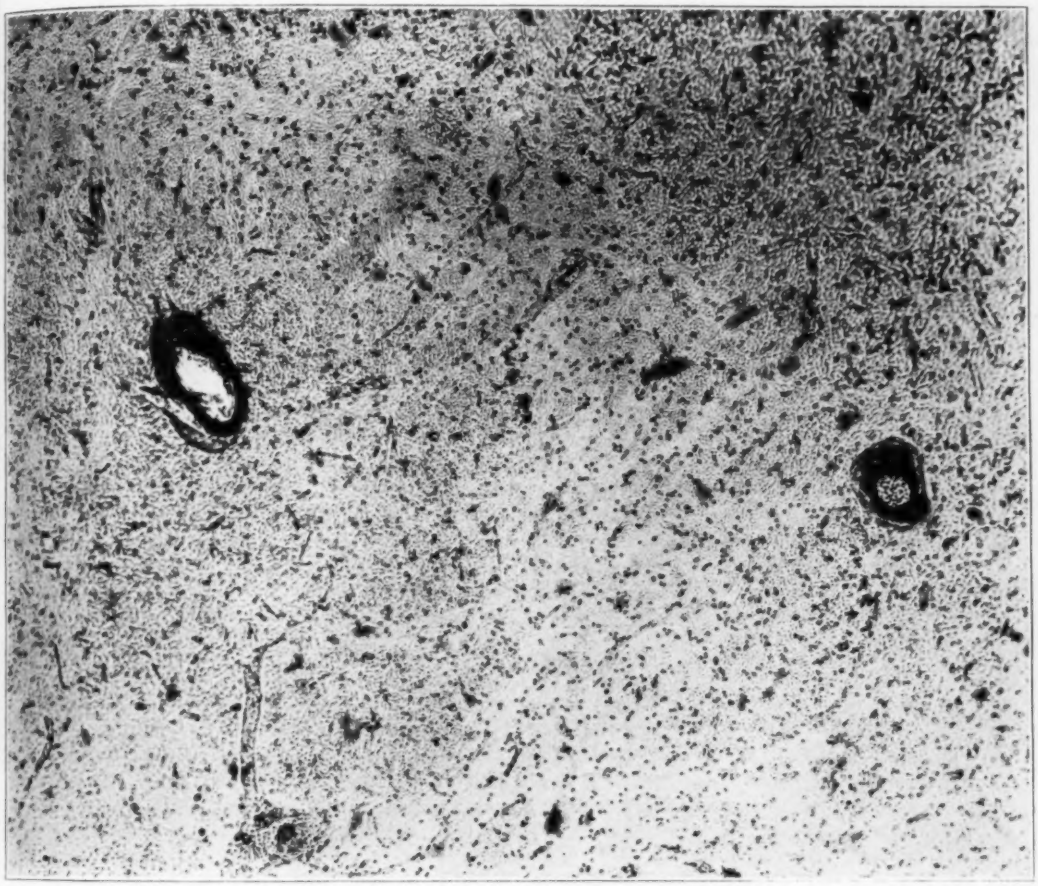

Fig. 7.—Section through the globus pallidus, showing calcification of the blood vessels and a decrease in the number of pallidal cells. Cresyl violet stain; × 50.

Postcentral and other parietal regions, temporal, hippocampal and occipital regions: Except for occasional poorly stained ganglion cells, sections showed nothing of note.

Basal ganglia: The white fibers of the globus pallidus took the myelin sheath stain poorly. Under a higher magnification some of the pallidal fibers, especially those on the right, were demyelinated. Some of the myelin sheaths were completely broken down, and others were swollen. A number of the vessels in the globus pallidus were markedly sclerosed and calcified (fig. 7). Small amyloid

bodies were also found. About the calcified vessels the pallidal cells were decreased, shrunken, had a homogeneous appearance and showed poor chromatin substance, and some were completely destroyed (fig. 7). In places there was a slight increase in the glia cells, consisting of protoplasmic astrocytes and occasional microglia and oligodendroglia. Most of these changes were found in the rostral and middle portions of the globus pallidus.

Corpus luysii: Sections showed the same changes as those of the globus pallidus, but they were not quite so marked. There were no calcified vessels in this structure, and the nerve cells were better preserved than those of the rostral end of the globus pallidus. In the same sections, the anterior limb of the right internal capsule showed a few vessels with round cell infiltration in the perivascular spaces.

Thalamus, paraventricular nuclei, substantia nigra and red nucleus: These were normal.

The region of the posterior commissure and pons: Sections showed slight demyelinization of some of the commissural fibers. The fibers of the pyramids stained poorly, and the corticobulbar fibers stood out more prominently. With a higher power, some of the posterior commissural fibers as well as the fibers of the pyramids were completely disintegrated. The smaller vessels showed moderate atherosclerotic changes. Some of the nerve cells within the pyramids showed mild degenerative changes. Sections in the region of the colliculi, cerebellum and pons showed marked thickening and fibrosis of the pia-arachnoid. Psammoma bodies were found within this fibrosed tissue. The white matter of the cerebellum did not take the myelin sheath stain very well; with a higher magnification occasional fiber disintegration could be observed. The architectural layers of the cerebellum were well preserved, except for poorly staining Nissl substance in the Purkinje cells.

Medulla oblongata: In the region of the twelfth nerve nucleus the pyramids were markedly demyelinated; most of the fibers were completely destroyed; some were broken down and showed signs of swelling. The cranial nerve nuclei of the medulla oblongata were intact. The same section showed a lacunar state of the white matter of the dentate nucleus.

Spinal cord: Sections at various levels showed demyelinization of both crossed and the right anterior pyramidal tracts (fig. 8). With a higher magnification, the changes previously described were found, except for an additional honeycomb appearance and a more advanced disintegration of the myelin. With the sudan IV stain the crossed pyramidal tracts were filled with compound granular corpuscles, which had a tendency to fill the perivascular spaces. In Bielschowsky preparations the axis cylinders were completely broken down and had a corkscrew appearance. The demyelinated areas were replaced by densely packed glia fibers. With cresyl violet, the anterior horn cells were decreased; some were shrunken, amorphous, stained deeply and did not contain any Nissl substance. There was a slight increase in the glia cells within the gray matter. These changes were observed throughout the sections of the spinal cord.

Microscopic Diagnosis.—The diagnosis was amyotrophic lateral sclerosis.

Comment.—Clinically, the patient in case 2 showed mental symptoms, a picture of extrapyramidal disease, closely simulating progressive lenticular degeneration, pyramidal tract signs and muscular atrophies; in other words, an unusual combination of amyotrophic lateral sclerosis with mental symptoms and a lenticular syndrome. The histopathologic changes were typical of amyotrophic lateral sclerosis, but in

addition there was definite involvement of the various cortical layers, and the pallidal structures showed changes characterized essentially by calcification of the vessels with secondary ganglion cell degeneration. There was no evidence of encephalitis.

CASE 3.—*History.*—E. G., a woman, aged 50, was admitted to the Montefiore Hospital on July 19, 1930, in a semistuporous condition, with a temperature of 104 F. She died the next day. In January, 1929, she had complained of pain in both shoulders, radiating to the lumbar region. In May of the same year she had had "nervous spells," difficulty in walking and spasticity of the lower extremities. In May, 1930, she had become drowsy and mentally confused. At two other hospitals a diagnosis first of multiple sclerosis and later of diffuse degenerative disease with mental symptoms was made.

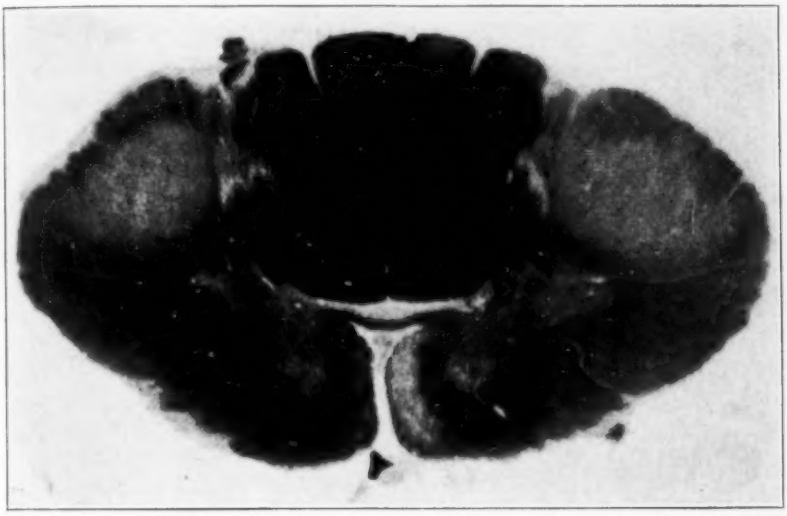

Fig. 8.—Section through the lower cervical cord, showing demyelinization of both lateral pyramidal tracts and the right anterior pyramidal tract. Myelin sheath stain (Weil modification); × 30.

Neurologic Examination.—The results were unsatisfactory because of the mental stupor. The patient presented a coarse and greasy skin, probable bilateral ptosis, right facial paralysis, spastic paresis of all four extremities, generalized deep hyperreflexia, bilateral Babinski sign, absent abdominal reflexes, dysmetria and a Parkinson-like facies with rigidity of the upper extremities, a tendency to an accoucheur position of the hands and catatonia. Mentally, the patient was confused, cooperated poorly, showed psychomotor retardation and was emotionally unstable.

Laboratory Data.—Except for a slight secondary anemia and a trace of albumin in the urine, all laboratory tests gave negative results.

Clinical and Anatomic Diagnoses.—The diagnoses were degenerative disease of the nervous system; generalized arteriosclerosis; arteriosclerosis of the coronary arteries; parenchymatous degeneration of the kidneys; purulent bronchitis, and bronchopneumonia.

Autopsy.—Gross Examination: Brain: The vessels were markedly congested. There was slight atrophy of the convolutions, more on the right, extending from the frontal to the postcentral gyri. The fissures in these areas were widely separated. The brain was cut vertically. In the region of the aqueduct there were a few small lacunae.

Spinal cord: The dura was slightly thickened, and its inner surface was studded with numerous calcareous bodies. There was a suggestive translucency of one of the lateral pyramidal tracts in the cervical, middorsal and lower dorsal

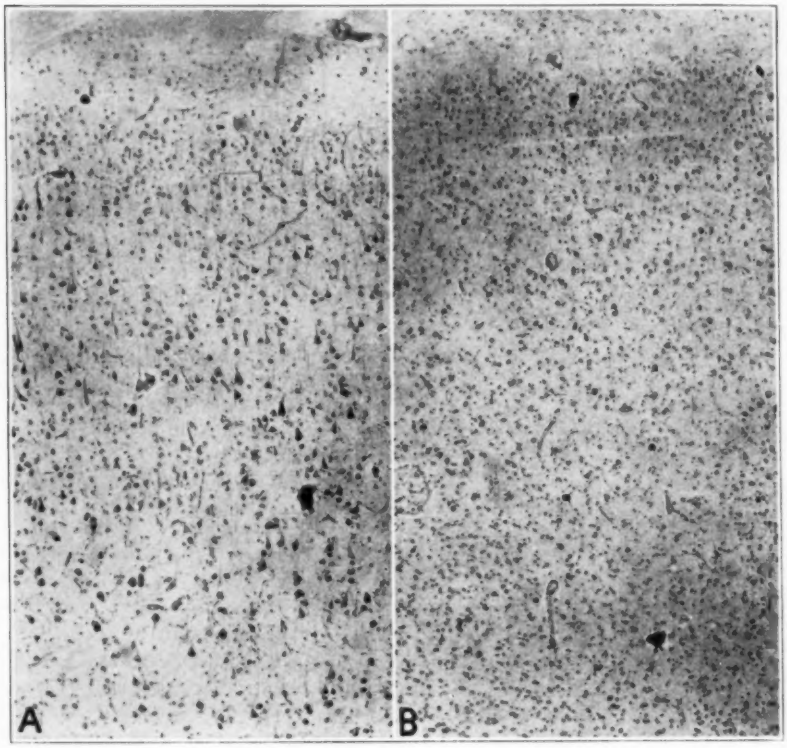

Fig. 9.—*A*, frontal area, showing scanty and poorly stained ganglion cells of the fifth and sixth laminae. *B*, postcentral gyrus, showing disturbance in the architectural arrangement of the cortical layers, except the first and second laminae. Poorly stained ganglion cells. Cresyl violet stain; × 40.

regions. Frozen and celloidin sections of the entire nervous system were stained by the same methods as in case 1.

Microscopic Examination: Frontal region: Sections through F_1, F_2 and F_3 showed normal meninges with moderate atherosclerotic vessels. The thickness of the gray matter was normal, and the white matter did not appear shrunken. There was no disturbance in the architectural arrangement of the layers of the cortex. However, the nerve cells of the fifth and sixth layers were fewer (fig. 9 *A*); they stained poorly and were totally devoid of Nissl substance; some showed chromato-

lytic changes. The nuclei of most of the ganglion cells were swollen and eccentric, and contained little chromatin. Throughout the fifth and sixth laminae there was hardly a normal nerve cell. A few of the ganglion cells of the third layer showed changes similar to those of the fifth and sixth. The glia cells were slightly increased in the third, fifth and sixth layers, and consisted of protoplasmic astrocytes and microglia. The white matter appeared normal. The larger vessels showed moderate atherosclerotic changes.

Precentral convolutions: Sections showed a falling out of the ganglion cells in practically all the layers, most noticeable in the fifth and sixth. The architectural layers were not so well preserved as in the frontal gyri. The more minute histologic changes in the ganglion cells were the same as in the frontal region. The giant pyramidal cells of Betz were fewer and showed chromatolytic changes.

Postcentral, other parietal and temporal areas: Except for marked disarrangement in the cortical architectural layers (fig. 9 *B*), sections showed the same changes as in the previous sections. The temporal lobes showed more marked changes than the other convolutions. The white matter was studded with numerous lacunae, which contained thin vessels with dilated perivascular spaces. The fibers did not take the myelin sheath stain as well as in the previous sections, although there was a lack of any breaking down of myelin. The architectural layers in the middle temporal lobes could barely be made out, and the falling out of ganglion cells and chromatolytic changes were more predominant in the third layer instead of the fifth and sixth as in the other regions. The hippocampus was loaded with numerous corpora amylacea, poorly stained ganglion cells and two calcified vessels.

Occipital lobes: Sections showed very slight changes.

Basal ganglia: With the myelin sheath stain the right globus pallidus had a lacunar appearance. The white fibers of the globus pallidus did not stain as well as normally; with a higher magnification, some of the fibers were completely demyelinated; this was best observed in the region of the calcified vessels. With cresyl violet, except for occasional destruction, most of the ganglion cells were fairly well preserved in the neostriatum, and the thalamic and paraventricular nuclei. In the globus pallidus, however, more so on the left, both the ganglion and the glia cells were fewer. The pallidal cells showed changes in acute and chronic stages, such as swelling, lack of chromatin, homogeneous appearance and occasional shrinkage and pyknosis; the nuclei were swollen, poor in chromatin and placed eccentrically. Throughout the pallidum, especially in the inner segment of the middle and caudal ends, numerous calcified blood vessels were found; in most of them the calcification was limited to the media and adventitia, sparing the intima, which was thickened. Occasionally, complete calcification of a vessel was observed. Most of the changes of the ganglion cells were found in the vicinity of the calcified vessels. There were no amyloid bodies as in case 2. The glia nuclei in these areas were slightly increased. The ventricles were not enlarged, nor was the ependyma thickened.

The corpus luysii, substantia nigra and red nucleus did not show any abnormalities. A few of the nerve cells in the oculomotor nerve nuclei showed evidence of pigment atrophy. The pons showed no changes except for a few poorly stained ganglion cells. The choroid plexus of the fourth ventricle was markedly calcified. The cerebellum was normal. In the medulla, sections through the twelfth nerve nucleus at the crossing of the lemnisci showed definite paling of the pyramids. The nerve cells of the tenth and twelfth nerve nuclei showed chromatolysis, shrinkage, vacuolization and pigment atrophy. The same changes were found in

the accessory olivary nuclei. The nerve cells of the locus caeruleus contained very little pigment.

Spinal cord: Throughout the cord there was marked demyelinization of both crossed pyramidal tracts, and, to a lesser extent, also of the left direct pyramidal tract (fig. 10). With a higher power, a number of the myelin sheaths were found to be completely destroyed and others swollen. Longitudinal sections, with Victoria blue, showed a definite increase of the glia fibers of the lateral pyramidal tracts; these had an isomorphous appearance. In the same areas, with the Bielschowsky method, the axis cylinders were broken down; some had a corkscrew appearance, and a few were fairly well preserved. With cresyl violet the anterior horn cells were fewer; some were markedly swollen, had a hemogeneous appearance, were devoid of Nissl substance and had swollen and eccentrically placed

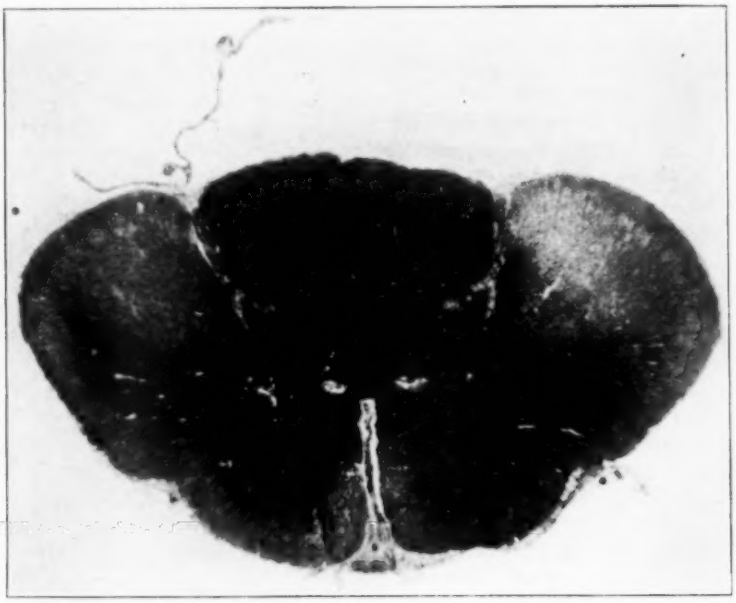

Fig. 10.—Section of the midthoracic region, showing demyelinization of the crossed, direct pyramidal and cerebellar pathways. Myelin sheath stain (Weil modification); × 25.

nuclei (fig. 11); those of the mesioventral group showed poor Nissl substance and atrophy. These changes in the ganglion cells were observed throughout the spinal cord, except in the sacral region, and were most marked in the thoracic region. The vessels were normal; the meninges were not thickened, and there was no evidence of any perivascular infiltration.

Microscopic Diagnosis.—The diagnosis was amyotrophic lateral sclerosis.

Comment.—Clinically, the patient in case 3 showed mental symptoms, Parkinson-like facies, rigidity of both upper extremities, with a fairly typical posture of the hands, and pyramidal tract signs. Atrophies of the muscles were not observed clinically. Histopathologically, there

were the characteristic changes in the pyramidal tracts and anterior horns, together with involvement of the ganglion cells of the fifth and sixth layers of various cortical gyri, and calcification of the pallidal vessels.

CASE 4.—*History.*—W. F., a man, aged 54, was first seen in May, 1929. The onset of the illness was indefinite, but was said to have begun with generalized

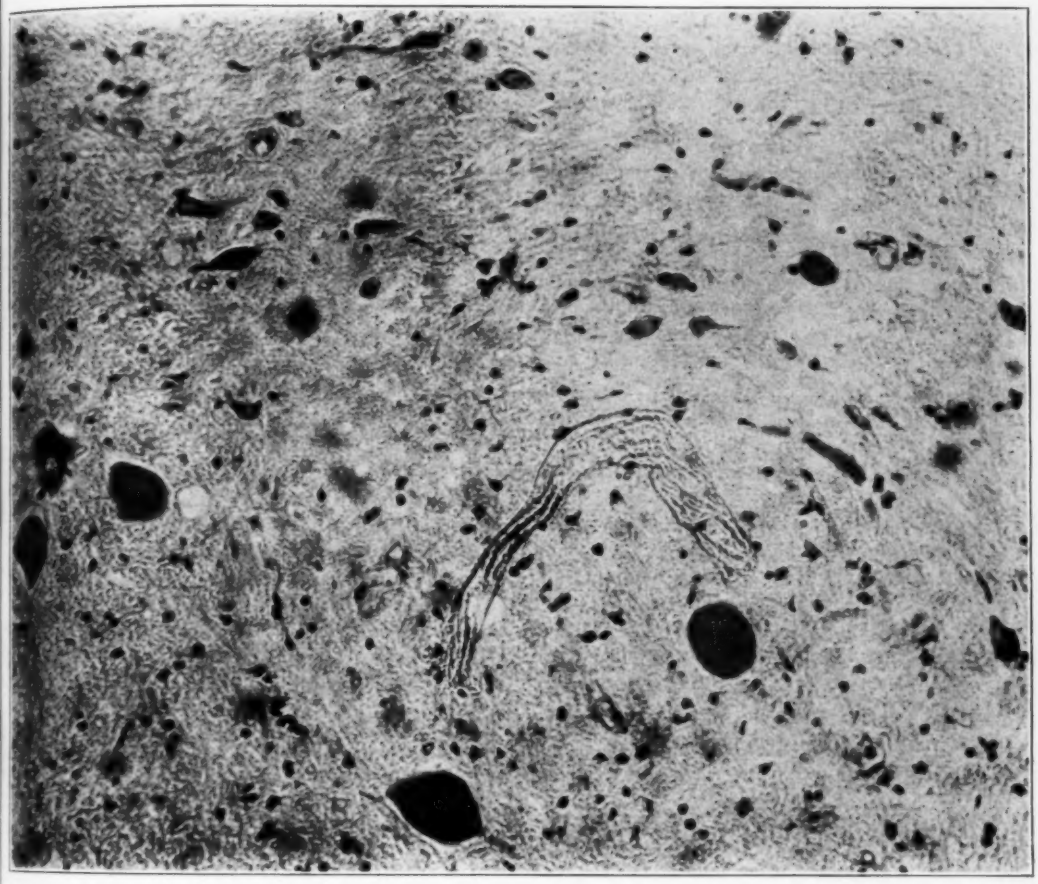

Fig. 11.—Section from the anterior horn, showing swelling of the nerve cells, homogeneous appearance and lack of Nissl substance. Cresyl violet stain; × 240.

twitchings of the muscles at some time in 1927. In 1928, the patient began to have difficulty in swallowing and choking spells due to the collection of mucus in the throat. The condition gradually became aggravated. Toward the end of the year mental symptoms developed for which he was admitted to a private sanatorium.

Physical Examination.—There was generalized atrophy of the body musculature, which was most marked in the muscles of the arms, shoulder blades and thenar eminences. Fibrillations were marked throughout. The deep reflexes were pres-

ent, but were somewhat diminished in the lower extremities. The abdominal reflexes were absent, and no Babinski sign was elicited. There were no sensory disturbances. There was a suggestion of facial atrophy; the uvula moved very little, and the tongue was atrophic, showed fibrillations and could be protruded only with difficulty. Other neurologic tests gave negative results. The patient had difficulty in swallowing and attacks of spasms of the muscles of the throat. Articulation was markedly impaired.

Mentally, the patient was confused but not completely disoriented; he had delusional trends of a paranoid character, which revolved about sexual exhibitionism on the part of a neighbor who threatened to corrupt the morals of his daughter. After a stay in the hospital of several months the patient was sent home, where his physical and mental condition gradually grew worse, and he died in May, 1930.

Comment.—The outstanding features in this case were the association of mental symptoms, essentially of a paranoid character, with a fairly typical form of amyotrophic lateral sclerosis.

Case 5.—*History.*—N. C., a man, aged 68, a laborer, was admitted to the Manhattan State Hospital with a history that for the past three years he had shown muscular weakness and progressive mental changes characterized by defective memory, disorientation, silly behavior, fabrication and aimless wandering.

Physical Examination.—There were marked emaciation (loss of 90 pounds [40.8 Kg.]), generalized increase of the deep reflexes, bilateral Babinski sign, atrophy of the small muscles of the hands, forearms and shoulder girdles and fibrillations in the tongue and the muscles of the upper arms and the shoulders. No other neurologic signs were observed. Mentally, the patient was disoriented in all spheres; he was confused and childish, and could not calculate or even count to twenty. Emotionally, he was labile but otherwise quiet and well behaved. He gradually showed increased mental impairment and muscular weakness; he died in July, 1930. The hospital diagnosis was senile psychosis with simple deterioration associated with amyotrophic lateral sclerosis.

Comment.—In case 5, too, there was amyotrophic lateral sclerosis, occurring at a rather advanced age, accompanied by definite mental changes.

Case 6.—*History.*—J. K., a woman, aged 56, who was admitted to the Manhattan State Hospital in April, 1929, had developed a gradual weakness of the right side in April, 1928. In October, 1928, her memory began to fail; she became irritable, showed changes in personality and developed delusions, stating that the neighbors listened to her conversations. Her family and personal histories were without significance, except that she had used alcoholic beverages excessively for a period of twenty years.

Neurologic Examination.—On admission to the Manhattan State Hospital, the patient showed bulbar speech, irregularity of the right pupil and beginning retinal arteriosclerosis. There were: atrophy and fibrillations of the tongue and interossei muscles, right foot-drop, absent knee jerks and a left Babinski sign. The blood pressure was 150 systolic and 90 diastolic.

Mental Examination.—The patient was cheerful, cooperative and coherent, but emotionally unstable. She was disoriented only for time. There was some reten-

tion defect. The memory for recent and remote events was fairly good. There was no tendency to hallucinations.

Laboratory Examinations.—These gave negative results.

Course.—On July 31, 1929, the patient began to show fits of uncontrollable crying. She died of lobar pneumonia in December, 1929.

Diagnosis.—The hospital diagnosis was psychosis with cerebral arteriosclerosis in a patient with amyotrophic lateral sclerosis.

Comment.—Case 6 is a somewhat atypical case of amyotrophic lateral sclerosis associated with mental changes, which were regarded as of cerebral arteriosclerotic nature.

COMMENT

In general, it is difficult to state whether the mental symptoms occasionally found in amyotrophic lateral sclerosis are part of the degenerative syndrome or chance associations. Considering the great number of cases that are entirely free from psychotic manifestations, except for depression as a reaction to any relentless and incapacitating disease, it is altogether questionable whether the syndrome commonly encountered is at all responsible for the psychosis. Add to this the usual absence of histopathologic changes in the brain, aside from the destruction of the Betz cells, and the question becomes even more difficult to answer. In order to say with assurance that the pathologic process causing amyotrophic lateral sclerosis is also capable of bringing about mental symptoms, the clinical picture would have to resemble an organic dementia and not a manic-depressive or other so-called emotional or psychogenic psychosis.

Many observers think that the mental symptoms have no relationship with the system disease and entirely dissociate the psychosis from the amyotrophic lateral sclerosis. Charcot made no mention of mental symptoms. Westphal [1] stated that he had observed schizophrenia, paranoid syndromes or a manic-depressive state, but that these were obviously unrelated. Westphal [1] and Zacher [2] mentioned the development of amyotrophic lateral sclerosis in the course of dementia paralytica. Pierre Marie [3] claimed that psychic symptoms were not rare in amyotrophic lateral sclerosis and considered them as part of the disease. They consisted of a tendency to laugh or weep without reason,

1. Westphal, A.: Schizophrenie Krankheitsprozesse und amyotrophische lateral Sklerose, Arch. f. Psychiat. **74**:310, 1925; Sclérose latérale amyotrophique developée dans le cours d'une paralysie générale, Compt. rend. Soc. de Psychiat. de Berlin, May 11, 1885; cited by von Bogaert, L.: Encéphale **20**:27, 1925.

2. Zacher: Ein Fall von progressiver Paralyse compliciert mit amyotrophischer lateral Sklerose, Neurol. Centralbl. **23**:551, 1886.

3. Marie, Pierre: Leçons sur les maladies de la moelle, Paris, Masson & Cie, 1892, p. 470.

exaggerated emotivity, childishness, credulity and, at the beginning of the disease, frequent symptoms of so-called neurasthenia. Raymond and Cestan [4] observed eighteen cases of amyotrophic lateral sclerosis which came to autopsy; in none of them were there delirious states, loss of memory or other intellectual deterioration. Two of their patients had spasmodic laughing and crying, but they were free from mental deterioration. They claimed that the patients became depressed in the terminal stages of the disease, when cachexia and bulbar signs set in, and were distressed as a result of the choking and difficulty in deglutition. Fragnito [5] described three cases with psychotic manifestations; one presented a picture of dementia; another, melancholia with suicidal tendencies, and the third had circular insanity (periods of depression followed by euphoric phases). Single cases of Charcot's disease associated with mental symptoms have also been recorded by Pilcz,[6] Cullerre,[7] Gentile,[8] Gerbert and Naville,[9] and Buscher.[10] More recently, Ziegler [11] reported some cases which, while not entirely convincing, also showed the association of mental symptoms with the amyotrophic syndrome. In most of these cases the psychoses belonged rather to the schizophrenias or the manic-depressive group and could not be said to have been true organic dementias.

Von Bogaert,[12] in an analysis of thirty-one cases of amyotrophic lateral sclerosis, in all of which the patients were under observation for a period of three years, found no psychosis in eighteen, changes in the affective state in three, and characteristic psychotic disturbances in ten. According to him, the first signs were disturbances in affectivity. The patient was discouraged, sad, anxious, thought of old worries and wept on the least provocation. The depression was occasionally accompanied

4. Raymond, F., and Cestan, R.: Dix-huit autopsies de sclérose latérale amyotrophique, Rev. neurol. **13**:504, 1905.

5. Fragnito, O.: I disturbi psichici nella sclerose laterale amiotrofica, Ann. di neurol. **25**:237, 1907.

6. Pilcz, A.: Ueber ein Fall von amyotrophische lateral Sklerose und Paranoia, Jahrb. f. Psychiat. u. Neurol. **17**:221, 1898.

7. Cullerre: Les troubles mentaux dans la sclérose latérale amyotrophique, Arch. de neurol. **31**:433, 1907.

8. Gentile: Disturbi psychici della sclerose laterale amyotrofica, Palermo, 1909; quoted by von Bogaert, L.: Encéphale **20**:27, 1925.

9. Gerbert, I., and Naville, F.: Étude histologique et clinique d'un cas de sclérose latérale, Encéphale **16**:113, 1921.

10. Buscher, J.: Zur Symptomatologie der sogenannte amyotrophischer lateral Sklerose, Arch. f. Psychiat. **66**:61, 1922.

11. Ziegler, L. H.: Psychotic and Emotional Phenomena Associated with Amyotrophic Lateral Sclerosis, Arch. Neurol. & Psychiat. **24**:930 (Nov.) 1930.

12. von Bogaert, L.: Les troubles mentaux dans la sclérose latérale amyotrophique, Encéphale **20**:27, 1925.

by obsessions and loss of sexual desire and interrupted by euphoric states. At times a true manic-depressive state set in; the patient then lost interest in his surroundings, became apathetic and talked little or badly, or he became euphoric, excited and talked or mumbled incomprehensibly. Later, memory defects for recent events and poor association set in. Finally, there was progressive intellectual impoverishment; the patient entered a confusional state, and the behavior resembled that observed in senile dementia. In some cases the disturbances in memory, attention and judgment were successive steps in a global demential syndrome, such as is seen in dementia paralytica or senile dementia. Von Bogaert claimed to have found in the spinal cord in case 23 a typical picture of amyotrophic lateral sclerosis associated with a lacunar state of the central gray nuclei. Von Bogaert,[12] Meyer [13] and Raymond and Cestan [4] apparently are the only ones who have studied histopathologically the spinal cords and brains of patients who had had amyotrophic lateral sclerosis associated with psychosis. Meyer [13] found changes in the brain similar to those seen in gas poisoning.

The first three cases reported by us showed both the clinical symptoms of psychoses and diffuse histopathologic changes in the brain to account for the mental pictures. Cases 2 and 3 showed, in addition to the cortical changes and the characteristic amyotrophic lateral sclerosis picture, involvement of the pallidal structures. Worthy of note were the association of spasmodic laughing and crying and the parkinsonism with the amyotrophic lateral sclerosis syndrome, not on the basis of chronic encephalitis as described by Wimmer.[14] Among thirty-four other cases that were observed by us clinically there were no symptoms of true organic psychoses. From our experience, therefore, we may say that a psychosis in amyotrophic lateral sclerosis is rare. The definite histopathologic changes in the first three cases, however, warrant the opinion that in them the degenerative process underlying the motor syndrome was also responsible for the organic psychosis. The three other cases reported by us, though of clinical interest, do not permit of such definite correlation.

CONCLUSIONS

In the vast majority of recorded cases, amyotrophic lateral sclerosis is not characterized clinically by definite psychotic manifestations. Most of the cases with such manifestations reported in the literature can better be explained by an incidental association with schizophrenic,

13. Meyer, A.: Ueber eine der amyotrophischen laterale Sklerose nahestehende Erkrankung mit psychischen Störungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **121**:107, 1929.

14. Wimmer, August: Chronic Epidemic Encephalitis, London, William Heinemann, 1924.

manic-depressive or paranoid syndromes or with simple depressions. In older patients the occurrence of definite organic dementia could with more reason be ascribed to the coexistent, but at the same time independent, general cerebral arteriosclerosis. In our cases and very few others the psychosis apparently was the cerebral expression of one generalized pathologic process.

ABSTRACT OF DISCUSSION

Dr. Foster Kennedy, New York: I wish to emphasize the value of this paper, in that it correlates defective structure with defective function. We have been accustomed, as neurologists, to correlate defective function with defective structure, but it seems to me, and to many others, that in diseases of the mind and in the deterioration of personality such correlation is not always emphasized. Cases such as this, in which organic disease of the brain is associated with deterioration of the emotional and intellectual life, help to develop a true pathology of the mind which as yet has no real existence.

Dr. Israel Strauss, New York: It is true that mental symptoms in amyotrophic lateral sclerosis are infrequently observed. I agree with the conservative attitude taken by the presenters in not wishing to ascribe to the cause of amyotrophic lateral sclerosis the changes they have observed in the brains of three patients, but I also wish to point out that since we are ignorant of the factor that produces amyotrophic lateral sclerosis, as we commonly know it, there is no reason for us to be hesitant in ascribing to that factor the power to affect other parts of the brain than those commonly affected as we know the disease.

UNUSUAL CASES OF SYPHILIS OF THE NERVOUS SYSTEM

A CLINICOPATHOLOGIC STUDY *

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Many German articles on the pathology of syphilis of the nervous system begin with an apology for taking up such a hackneyed subject. Strangely enough, for more than a decade, except for the changes resulting from malarial treatment, the English literature is relatively silent on what is one of the most important subjects for the clinical neurologist.

In the textbooks, syphilis of the nervous system is divided into its well known types. There is first a general division into the parenchymatous and the meningovascular forms. The former is the type known as dementia paralytica; it can be further subdivided into typical and atypical forms, including the juvenile, stationary and Lissauer types. The meningovascular form can be subdivided into the pure meningeal form, with and without gummatous involvement, and vascular syphilis of various types. For descriptive purposes a classification of this sort is necessary and convenient, but cannot always be strictly adhered to. While the pure forms of the foregoing types are the rule, there occur combinations of them so that the resulting picture is at times confusing. It is for this reason that we have selected for this report a group of unusual cases of syphilitic involvement of the central nervous system.

REPORT OF CASES

CASE 1.—*Status epilepticus with a history of alcoholism, a previous syphilitic infection and an injury of the head. No neurologic symptoms. Pathologic diagnosis: meningo-encephalitis gummosa of the right frontal lobe.*

Clinical History.—H. S., a white man, aged 32, was admitted to the Philadelphia General Hospital, in the service of Dr. C. W. Burr, on Nov. 23, 1929. He had been a soldier in the World War, serving in France, and had received an injury of the head, details of which were unobtainable. There was a history of syphilitic infection, but the date was not known. He had been a free user of alcohol for

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* From the Laboratory and Wards of the Philadelphia General Hospital and Temple University Medical School.

many years. There was no history of epilepsy in the family. He had had influenza and rheumatism some years before this illness. Six months before admission, he had had several epileptiform seizures, all of which were generalized and consisted of tonic and clonic movements of the body muscles, associated with frothing at the mouth and biting of the tongue, marked cyanosis and involuntary passage of urine.

Examination.—On admission, the patient was in status epilepticus. The pulse was rapid in rate and small, and the heart sounds were weak. There were no murmurs. The pupils were round, equal in size, and reacted to light and in accommodation. There were no palsies of the extra-ocular muscles, and the eyegrounds were normal. The tendon reflexes of both upper and lower extremities were present, equal and active. He could not be aroused. The blood pressure was 100 systolic and 70 diastolic. He failed rapidly. The seizures continued with short interruptions until death on the third day after admission (November 25).

Laboratory Studies.—The Wassermann reaction of the blood was 4 plus. The spinal fluid was clear. There were 12 cells per cubic millimeter, with a negative globulin test, and the Wassermann reaction was negative with several antigens. The urea nitrogen of the blood was 23 mg.; the sugar, 135 mg.; the white cell count was 9,400. While the patient was in the hospital the temperature varied from 99 to 104 F.; the pulse rate was from 90 to 170; the respiratory rate was from 24 to 65.

Pathology.—Gross Examination: Gross examination of the brain showed an increased density and enlargement of the right frontal pole, with light adhesions to the dura in the anterior fossa. When the dura was separated from the orbital surface, there was noted a collection of yellowish material the nature of which was not determined by gross study.

Microscopic Examination: The lesion noted grossly showed as follows: The pia-arachnoid over the entire right frontal lobe contained a great number of round cells, mainly of the lymphocytic type, but with a definite increase in fibroblasts. Over an area of about 2 cm. of the orbital and mesial surface of the right frontal lobe were intense thickening and fibrosis of the pia-arachnoid, so that at first glance it resembled the dura (fig. 1). There was, in addition, marked infiltration with lymphocytes in and between the connective tissue fibers. In most of this area there were adherence to and penetration into the cortex, so that it was beyond recognition down to the subcortex. In this area also there was an intense increase in young fibroblasts, with numerous ganglion cells still present, some of which contained brownish pigment, irregularly distributed through the granulomatous tissue. A great number of lymphocytes were also present. The bulk of the mass, however, was made up of connective tissue and glia. The latter consisted particularly of macroglia of the protoplasmic type. The connective tissue increase was beautifully brought out in the Klarfeld preparations (fig. 2), which also gave an idea of the tremendous increase in the small vessels and the extreme density of the connective tissue feltwork. There were but few large blood vessels within the limits of the granulomatous mass, and these showed no changes. The small vessels in the surrounding tissue showed a marked endarteritic change. A definite area of necrosis with liquefaction was found in relation to the dural attachment and explained the yellowish puslike material noted grossly.

Diagnosis.—The diagnosis was meningo-encephalitis gummosa of the right frontal lobe.

Comment.—From the clinical point of view, several features are important: 1. The onset of convulsions in a patient over 30. This makes one suspicious of syphilis or of a gross lesion as an etiologic factor.

2. The occurrence of status epilepticus. Collier [1] has recently stated that lesions of the frontal lobe often cause status, and that he has never seen it occur with a lesion in any other region of the brain. Collier does not mean by this that in all cases of status a gross frontal lesion is to be postulated, but that in the presence of a gross lesion the frontal area is the usual site of involvement. In our own experience this has been borne out fairly well. In only one case did we find no gross lesion of the brain. When a gross lesion was present, it was in the frontal area

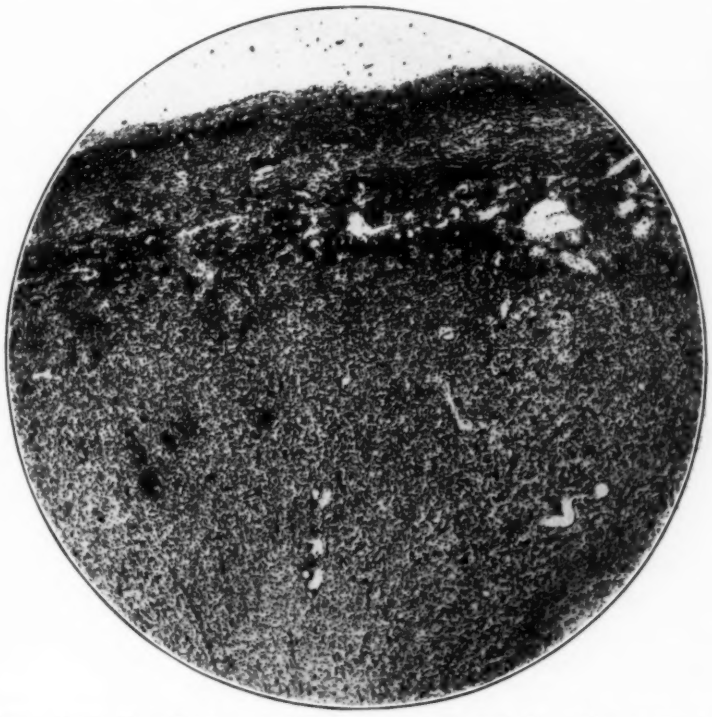

Fig. 1 (case 1).—Meningo-encephalitic gumma. Toluidine blue stain, showing marked chronic adhesive and inflammatory lesion of the frontal lobe

in all but one case. 3. The absence of all clinical signs of syphilitic involvement of the nervous system. Particular mention must be made of the absence of Argyll Robertson pupils, the normal reflex activity and the normal cranial nerves.

From the serologic angle, this patient showed a strongly positive blood reaction with negative reactions of the spinal fluid.

1. Collier, J.: Diagnosis of Frontal Tumors, Brit. M. J. **2**:289 (Aug. 17) 1929.

Pathologically, a typical gummatous process was present. There is no doubt that today gross syphilitic granulomas are rare. Jakob [2] found only five gummas in his vast material from 1919 to 1929, inclusive. Bagdosar,[3] from Cushing's clinic, in reviewing 15,000 verified tumors of the brain, was able to find only eight gummas. In our own laboratory, gross syphilitic granulomas have been discovered nine times in over 5,000 autopsies.

From the histologic angle, the structure of a gumma is too well known to require detailed description. The only point that might be discussed is its differentiation from a granuloma due to the tubercle bacillus. As a whole the structures are remarkably similar, and at times they may offer difficulties in differentiation. One of the chief distinguishing features concerns the blood vessels. In syphilis one looks for the characteristic Heubner type of endarteritis, with its uniformly proliferated intima, without degenerative changes, and the presence of chronic inflammatory elements in the perivascular spaces. In tuberculosis, the changes in the vessels likewise consist of an invasion of the perivascular adventitial spaces with lymphocytes and plasma cells. While the media may be spared, it is often infiltrated. The changes in the intima are, however, characteristic and consist of a marked edema, so that the intimal lining is lifted away from its bed on the elastic lamina and in this edematous space are degenerated cells of various types (macrophages, polymorphonuclears and lymphocytes). This is the so-called panarteritis tuberculosa. So great may the intimal swelling be that occlusion of the lumen may and does result. Nonne and Luce,[4] Askanazy [5] and Kirschbaum [6] have described tuberculomas within the intima itself, but these are extremely rare.

The second differential point is the overwhelming increase in connective tissue in the gumma as shown by the presence of black-staining fibrils by the tannin-silver method (Klarfeld) (fig. 2). This is definitely in contrast to the very moderate connective tissue proliferation in tuberculomas.

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2. Jakob, A.: Handbuch der Psychiatrie, Vienna, Franz Deuticke, 1929, vol. 2, pt. 1; Ueber der Befund von miliären Gummen bei der Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:313, 1926.

3. Bagdosar, D.: Le traitement chirurgical des gummes cérébrales, Rev. neurol. **2**:1 (July) 1929.

4. Nonne and Luce: Pathologische Anatomie des Gefässes, in Flatau, E.; Jacobsohn, L., and Minor: Handbuch der pathologischen Anatomie des Nervensystems, Berlin, Julius Springer, 1904.

5. Askanazy, M.: Die Gefässveränderungen bei der akuten tuberkulösen Meningitis und ihre Beziehungen zu den Gehirnläsionen, Deutsches Arch. f. klin. Med. **99**:333, 1910.

6. Kirschbaum, W.: Ueber die Tuberculose des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **66**:283, 1921.

The situation of the gumma in our case is noteworthy. It began probably as a focal syphilitic lesion in the meninges, with secondary invasion into the brain substance. It is interesting to note that it occurred in a part of the subarachnoid system where the fluid is relatively scanty and stagnant, and this may even explain the negative serology of the spinal fluid.

The presence of a focal gummatous lesion calls for surgical treatment. It has been the experience of most clinicians that they do not "melt down" with antisyphilitic treatment.

Fig. 2 (case 1).—Tannin-silver (Klarfeld) stain of the same region as in figure 1, showing an intense increase of silver fibrils and vessels in the gumma.

The occurrence of a gumma after trauma has been considered possible by various authors. Whether or not a focal trauma causes a locus minoris resistentiae is speculative. True enough, in our case there was an indefinite history of a trauma of the head many years before, but the exact site of the injury is unknown.

CASE 2.—*Headache, diplopia and weakness of the left side for eight days. Seven days later, ptosis of the right lid, stupor and weakness of the right side. Serologic tests positive. Pathologic diagnosis: meningovascular syphilis with gumma of the pons and midbrain.*

Clinical History.—J. D., a colored woman, aged 27, was admitted to the Philadelphia General Hospital, in the service of Dr. D. J. McCarthy, on Nov. 2, 1928. She complained of headache, pain through the right eye, double vision and weakness of the left arm and leg. She had had "grippe" eight weeks previously, associated with dull headache, fever and general malaise. During convalescence, one week later, while the patient was cooking supper, the left arm "went to sleep" for ten minutes. About an hour later, this condition returned for five minutes. After another hour, the numbness returned and remained permanently. On the next morning, the left leg was "weak" and she could not move the foot. This condition did not improve.

In childhood the patient had had the usual children's diseases. Eight years previous to admission, there was swelling of the joints with pain and fever. Following this illness, dyspnea on exertion was present. The tonsils were removed six years before. She was married, and there had been one miscarriage, one living child, and one child died at birth. She was a heavy smoker and used alcohol to excess.

Examination.—The patient was well nourished. The right pupil was slightly larger than the left; both reacted to light and in accommodation. There was slight weakness of the lower part of the left side of the face, and the tongue deviated slightly to that side. The lungs were normal. The heart was slightly enlarged to the left and downward, and there was a loud systolic murmur at the apex. The blood pressure was 130 systolic and 80 diastolic. There was partial loss of power in the left arm and leg. She dragged the left leg in walking. There was no Romberg sign. Coordination was normal in all extremities. There was normal stereognosis. The tendon reflexes were increased on the left as compared with those of the right. The Babinski sign on the left was not absolutely definite. There was no ankle clonus. Touch and temperature sensations were everywhere normal. Vibration sense was normal.

Laboratory Studies.—The urine contained a trace of albumin with many hyaline and granular casts. Examination of the blood showed: hemoglobin, 12.6 Gm.; white cells, 7,500; urea nitrogen, 10 mg.; sugar, 100 mg. The Wassermann reactions of the blood and spinal fluid were 4 plus. There were 128 lymphocytes per cubic millimeter in the spinal fluid, with an increase of globulin and a gold curve of 2335544321. The spinal fluid pressure was 9 mm. of mercury.

Course.—A few days after admission to the hospital, the jaw muscles became spastic and stiffness of the neck appeared; speech became incoherent, and the patient complained of headache.

On November 7, ptosis of the right upper lid was observed for the first time, with weakness of the right external rectus muscle; the left internal rectus muscle was also weak. The patient was unable to protrude the tongue or to pucker the lips. The spinal fluid pressure was 12 mm. of mercury; there was no definite block, but the pressure, which rose to 40 mm. on jugular compression, took thirty seconds to return to normal. The eyegrounds showed haziness of the nasal side of each disk.

On November 9, the patient was unconscious. The left eye deviated to the left. There was slight loss of power on the right side, which was flaccid; the left side was spastic. There was a Kernig sign on the right; the Babinski sign was absent on both sides. The patient died on this day.

Pathology.—Gross Examination: The brain was small (weight, 1,130 Gm.). There was marked sclerosis of the basal vessels, which were very small; their walls were whitish and contained numerous plaques. On cross-section of the pons, anteriorly there was a dense area of fleshy appearance which was adherent to the

pia-arachnoid. This lesion extended deeper in the basis pontis on the right side. On the right also, there was an area of softening, 0.75 cm. in diameter, posterior to the dense area, which practically obliterated the pyramidal tract on that side. These lesions were located practically entirely in the middle and upper half of the pons and extended into the lowermost part of the midbrain. The fourth ventricle was granular.

Microscopic Examination: Cross-sections of the pons at the point of maximum involvement showed: The basilar artery presented a most intense thickening of its entire coat as a result of proliferation of the connective tissue cells, without degenerative manifestations (fig. 3*A*). The media was completely destroyed and

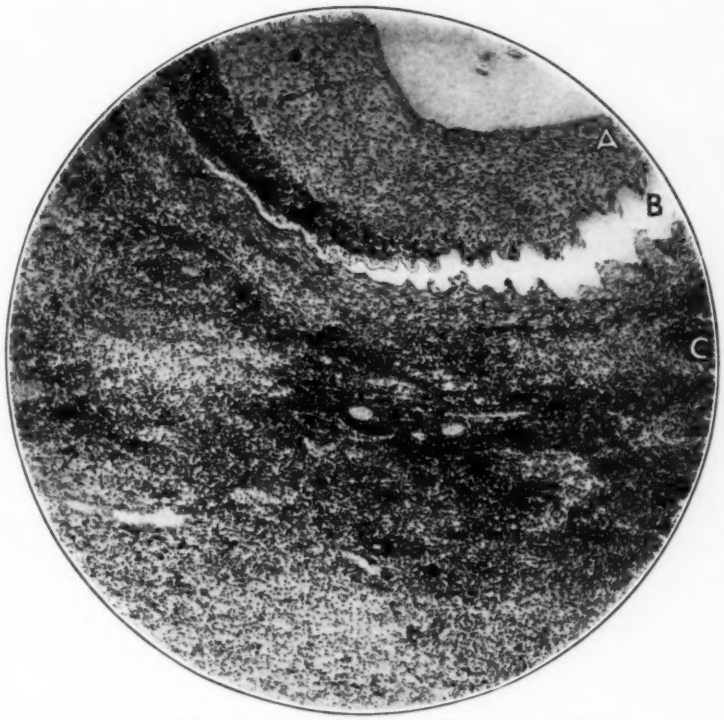

Fig. 3 (case 2).—Gumma on the anterior portion of the pons (toluidine blue stain). A portion of the wall of the basilar artery is shown with Heubner's endarteritis. At *A* is markedly thickened intima; at *B*, elastic lamina; at *C*, markedly invaded adventitia gradually merging into pontile tissue.

in its place was an inflammatory lesion made up of plasma cells and, particularly, lymphocytes with numerous fibroblasts. This inflammatory exudate penetrated the intima, and the elastic lamina was ruptured at one point. The adventitia was invaded with the same type of cells as the rest of the vessel wall. There was thus formed what was really a gummatous lesion, especially on one side of the vessel wall. The inflammatory lesion was continued from the vessel to the meningeal space and penetrated into the basis pontis (fig. 3*C*). In the center of the lesion was a homogeneous necrotic area, and around it was the intense inflammatory exudate. Klarfeld preparations (fig. 4) brought out positively the intense fibrosis

that had taken place within the lesion. Unna-Pappenheim preparations showed at a glance the increased numbers of plasma cells. Posterior to the inflammatory lesion on the right side was an area of softening, with the remains of gitter cells in the midst of the very spongy tissue. The contiguous vessels were collared with round cells, many of which still contained greenish and yellowish pigment particles. A glial increase was present throughout the entire cross-section of the pons. On the right, the inflammatory lesion had extended laterally and involved the fifth nerve throughout its entire intracranial course.

Diagnosis.—The diagnosis was meningovascular syphilis, with gumma of the upper part of the pons and the midbrain.

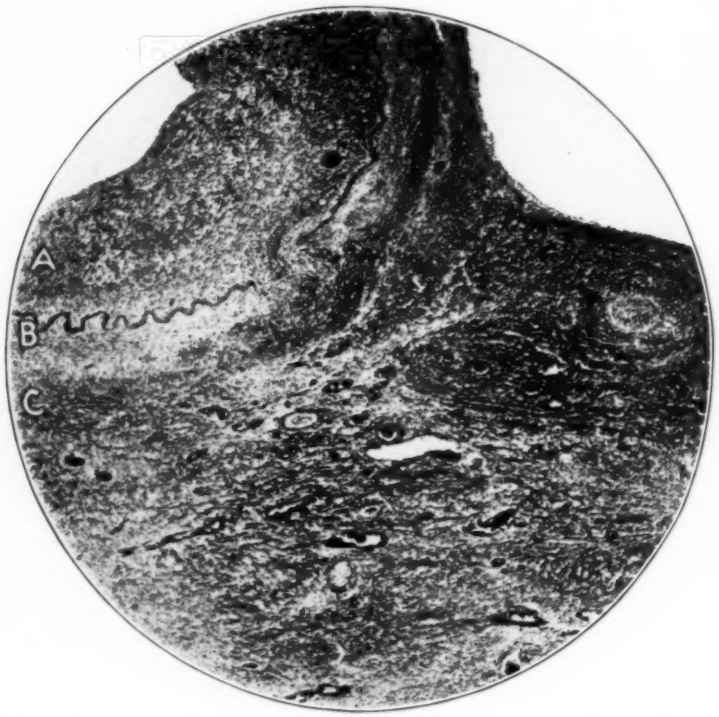

Fig. 4 (case 2).—Same field as represented in figure 3 (Klarfeld stain). Rupture of the elastic lamina can be seen in this preparation. There is a marked fibrillary increase.

Comment.—From the clinical standpoint, the occurrence of bilateral symptoms in a young syphilitic person at different times might suggest multiple vascular lesions. At autopsy, a gumma of the anterior part of the pons and adjoining midbrain was found. This fully explains the clinical picture. It was part of a general syphilitic involvement of the entire brain. It has been thought that lesions of this sort begin in the meninges and penetrate into the nerve tissue secondarily only after a mild devitalization from vascular interference.

The location of the lesion here is somewhat different from usual; it is usually in the interpeduncular space. In the latter cases the symptom complex begins with third nerve signs; in our case the third nerve signs appeared late.

Gummas of the basilar region may involve any or all of the cranial nerves and even the pituitary, as reported by Kufs.[7]

CASE 3.—*Inability to walk for one year. Pain in the back and legs for two years. Hyperesthesia of the legs. Spinal fluid serology 4 plus. Pathologic diagnosis: meningomyelitis, with gumma on the right side of the lumbar cord; annular degeneration of the cervical cord.*

Clinical History.—P. P., a white man, aged 34, was admitted to the Philadelphia General Hospital, in the service of Dr. M. J. Burns, on Sept. 17, 1929, complaining of inability to walk for twelve months. Two years previously he had begun to have pains in the lumbar area; six months later, he began to limp and rapidly lost power in his legs, so that he became unable to walk. He was in bed for three months before admission. There had been a persistent dull pain in both legs during the past year, and as the legs grew weaker he had had burning with and frequency of urination. At times there was retention of urine. He had a sensation of a belt tightening about the lower part of the body when he attempted to straighten the legs. He had had a chancre twelve years previously. The family history was without significance.

Examination.—The pupils were slightly irregular and reacted sluggishly to light and in accommodation. Slight movement was possible in the right leg and thigh, but the left leg was paralyzed completely. There was incontinence of urine. Pain and touch sensations were lost in the left leg and impaired in the right. The arms were normal. The knee and ankle jerks were increased on the right, but absent on the left; the triceps and biceps reflexes were normal on both sides. There were ankle clonus and a Babinski sign on the right; these were absent on the left.

Course.—The patient was given tryparsamide regularly, but did not improve. Gradually, atrophy of both lower extremities developed. Intensive antisyphilitic treatment was continued, but the patient gave no clinical response. The weakness continued until the time of death.

Laboratory Examinations.—The urine contained a faint trace of albumin. Examination of the blood showed: hemoglobin, 14.9 Gm.; red cells, 5,070,000; white cells, 8,900; Wassermann reaction, negative with both cholesterol-fortified and alcoholic antigens. The spinal fluid was clear; there were: 4 cells per cubic millimeter, 1 plus globulin reaction, 4 plus Wassermann reaction; colloidal gold curve, 1355332100.

Pathologic Examination.—Grossly, the brain showed a moderate matting together of the frontal lobes. In the cord the dura was somewhat thicker than normal, with adherence to the cord substance in the lumbar region to such a degree that separation was impossible.

Microscopically, there were marked thickening and matting together of all the coverings of the cord, which in turn were adherent to the cord substance in the lumbar region on the right side. At this point there was an inflammatory reaction, with the presence of lymphocytes not only in the meninges but also extending into the spinal cord substance, with consequent degeneration and gliosis of practically

7. Kufs, H.: Beiträge zur atypischen Paralyse und zur Endarteritis syphilitica der kleinen Rindengefässe, Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:518, 1926.

one-half the cord. In the cervical region of the spinal cord there was degeneration of the columns of Goll, which was as intense as if the lowermost roots had been cut completely across (fig. 5). Here also was a rim of degeneration around the entire cord, similar to the so-called annular, or marginal, degeneration. It dipped down and involved the pyramidal tract on each side of the anterior fissure. It did not extend deeper in the cord substance in the area occupied by the direct cerebellar tracts, so that an ascending degeneration could be ruled out in this case. A marked involvement of the meninges at this level was not found, and only an occasional group of chronic inflammatory cells was discovered. The blood vessels showed Heubner's endarteritis, especially in the small and medium-sized vessels.

Microscopic Diagnosis.—The diagnosis was meningomyelitis, with gumma over the right side of the lumbar cord and annular degeneration of the cervical cord.

Comment.—From the clinical standpoint, the presence of an incomplete Brown-Séquard syndrome would make one suspicious of either

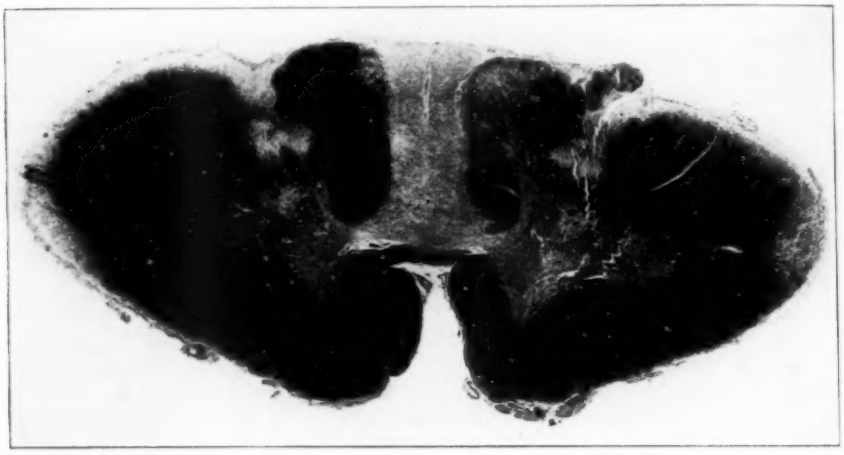

Fig. 5 (case 3).—Myelin sheath stain of the cervical cord, showing ascending degeneration in the posterior columns and a marginal or rim degeneration.

a cord tumor or syphilis. The symptomatology was explained completely by the gummatous lesion involving all the meninges and penetrating the right side of the cord in the lumbar area. This, in itself, would not make the case worthy of report. The unusual observation, however, was the presence of a circumferential or annular degeneration in the cervical region (fig. 5). That this was not the result of a retrograde degeneration can be seen easily by the presence of involvement of the anterior pyramidal tracts. That this is not a common lesion is shown by the fact that in the literature only single cases have been reported by Merle,[8] Lannois and Porat,[9] Raymond and Cestan,[10] Alquier

8. Merle, E.: Rev. neurol. **17**:878, 1909.

9. Lannois and Porat: Rev. de méd., Paris **26**:567, 1906.

10. Raymond and Cestan: Méningo-myélite marginale progressive, Encéphale **4**:1, 1909.

and Touchard,[11] Allen,[12] Martin [13] and Spiller. In textbooks, a pathology of this sort is usually postulated in the Erb type of syphilitic involvement of the cord.

An explanation of this type of involvement has been difficult to find as is shown by the numerous theories proposed. This has been discussed at length by Martin. It will suffice here to state that three important theories stand out: (1) the poison reaches the tissues involved through lymphatic channels; (2) the poison passes through the blood stream into the small circumferential vessels of the cord; (3) the injurious material diffuses directly from the subarachnoid space against the marginal areas of the cord.

In our case the adherence of the meninges to the cord occurred in the lumbar region, with a focal gumma at this point. In the cervical region, however, where the annular degeneration occurred, no such meningeal adhesion was present. It is true that the smaller vessels showed narrowing, the result of syphilitic changes, but this was not limited to the vessels of the periphery.

CASE 4.—*Gradual loss of power of the legs following a fall, fifteen months previously, associated with pain. No spinal block, and no evidence of a level lesion. Serology negative. Pathologic diagnosis: syphilitic vascular disease of the cord with multiple areas of softening.*

Clinical History.—L. A., a white man, aged 50, was referred to Dr. W. G. Spiller because of loss of power of the legs and weakness about the lower part of the back and the hips. He had been well until Aug. 18, 1926, when his foot slipped while he was moving a coal conveyor. He did not fall, but felt a sharp pain in the lower part of the back and the hips. The pain gradually became severe, starting in the hips and radiating down the legs to the toes, but was constant and walking increased it. In December, 1927, crutches became necessary in walking. There was no improvement in the pain, and gradually the patient grew weaker. He was confined to bed after May, 1928. He made no complaint of sensory disturbance of the legs, but had had poor control of the bowels and urine since the injury. Frequent catheterization became necessary. He was able to feel the bowels moving, but not the bladder until the urine touched his leg. His sight had been failing for a few years, and he had been deaf for five or six years.

Neurologic Examination.—The biceps and triceps reflexes were prompt and equal; the patellar and achilles reflexes were sluggish; there was no clonus and no definite Babinski sign. Touch sensation was slightly diminished over both legs to the hips; the trunk and upper limbs had normal sensation; position sense of the toes was normal; pain sensation was present over the inner one fourth of the buttock, extending down over three fourths of the posterior surface of both thighs; heat and cold senses were lost in the area of pain; vibration sense was diminished in both legs. The legs were markedly weak.

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11. Alquier and Touchard: Encéphale **4**:404, 1909.

12. Allen, A. R.: Combined Pseudosystemic Disease with Special Reference to Annular Degeneration, Univ. Pennsylvania M. Bull., January, 1905, p. 1.

13. Martin, J. P.: Amyotrophic Meningo-Myelitis, Brain **48**:153, 1925.

Laboratory Examinations.—Examination of the blood showed: hemoglobin, 70 per cent; red cells, 4,040,000; white cells, 7,200; Wassermann reaction, negative with several antigens. The spinal fluid showed a negative Wassermann reaction on all occasions. Roentgenograms of the spine were normal. Iodized poppy seed oil 40 per cent injected intracisternally settled to the lower part of the spine without obstruction.

Course.—The patient became completely paralyzed from the waist down, with retention, two months prior to death. From frequent catheterization he developed pyelonephrosis as a result of which he died.

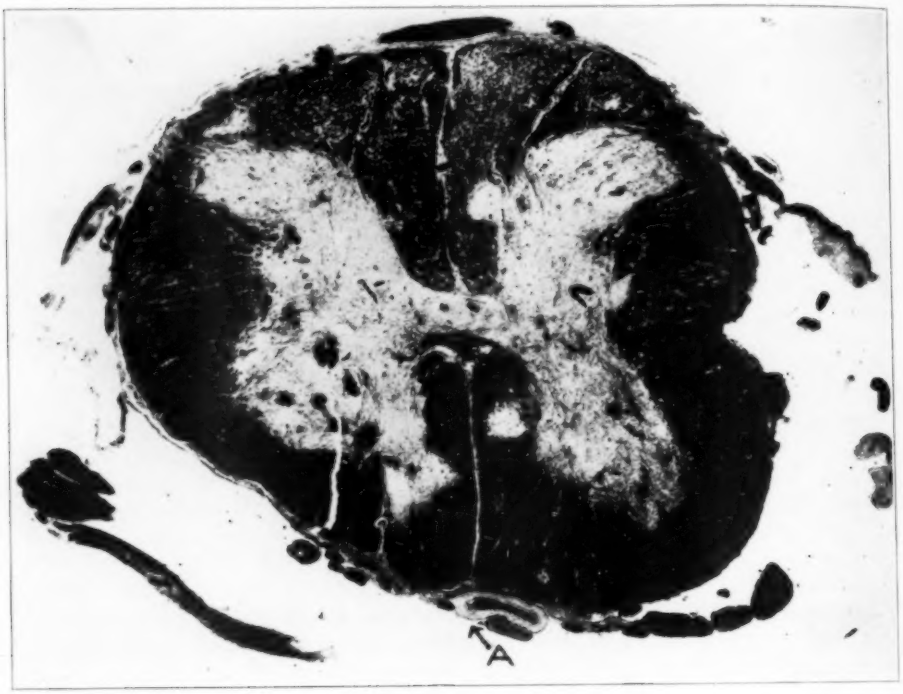

Fig. 6 (case 4).—Pure vascular spinal syphilis of Henneberg, showing multiple areas of softening due to vascular occlusion within the spinal cord substance. The anterior spinal artery can be made out, with its markedly thickened intima of syphilitic type (*A*).

Pathology.—Gross examination of the spinal cord showed nothing of note. Microscopically, the important features were: 1. By the Weigert stain (fig. 6), the posterior columns were seen to be partially demyelinated. This was of the type seen in tabes; the degeneration tended to approach the midline (column of Goll) as the cord was ascended. The lateral pyramidal tracts showed bilaterally a mild degeneration. 2. The unusual feature was the presence of small areas of degeneration, with secondary gliosis in the distribution of the small vessels. These areas can be seen in figure 6. They were small, irregular and not in the position of anatomic tracts. They resembled to a remarkable degree the patches seen in multiple sclerosis, because of their irregularity, sharpness of outline and nonanatomic

location. The areas differed in no way from "Erweichungsherde," or areas of softening in the brain in severe arteriosclerosis. While the degeneration of the posterior columns was systemic, that of the lateral columns consisted of numerous foci of softening and secondary gliosis. 3. Heubner's type of endarteritis was present in portions of the anterior spinal artery, as well as thickening and hyalinization of the walls of the small vessels (fig. 6 *A*). Fibrosis was evident in the meninges, but only occasionally was round cell infiltration observed.

Microscopic Diagnosis.—The diagnosis was syphilitic vascular disease of the cord, with multiple areas of softening.

Comment.—From the clinical standpoint, while syphilis was strongly suspected by Dr. Spiller, serologic study always gave negative results. While the patient dated the symptoms directly to a minor accident, it was learned that he had had bladder symptoms before. It was probable that the symptoms had come on "in attacks," not unlike those seen in pseudobulbar palsy.

Few cases of this sort have been reported in the literature. Henneberg [14] called attention to this type of change under the name of "reine vasculäre Spinallues," which he reported in only one case.

At first glance the patches of degeneration in myelin sheath preparations might be mistaken for the patches of multiple sclerosis, but their evident relationship to the vessels and the vascular pathology are sufficient to rule out disseminated sclerosis, in addition to the discovery of actual microscopic softening in cell preparations. The presence of typical chronic syphilitic endarteritis favors, of course, the diagnosis here made.

It has been our experience that vascular disease, whether due to syphilis or to old age, is not nearly as common in the spinal cord as in the brain. This we have explained on the basis of the peculiarities of the circulation, because both the anterior and the posterior spinal arteries are not in the direct line of current flow of the vertebral vessels. This may also explain the extreme infrequency of metastatic lesions of all sorts to the spinal cord.

The usual pathologic changes in the cord from vascular disease are due mainly to involvement of the larger vessels and produce more or less complete transverse lesions, while in our case the smaller vessels were mainly at fault and hence small lesions resulted.

In the literature one finds that in the few cases reported the serology has been negative, as in our own case. The fact that the patients do not respond to antisyphilitic medication should not be used as an argument against the syphilitic etiology. In our case, from the appearance of the blood vessels, there is no doubt as to the syphilitic basis.

14. Henneberg, H.: Reine vaskuläre spinal Lues, Berl. klin. Wchnschr. **57:** 1026, 1920.

CASE 5.—*Hydrocephalus from birth, with mental deficiency; marked personality changes for two years. Convulsions for nine months. Legs spastic for one year. Inability to speak for three months. Serology positive. Anatomic diagnosis: meningovascular syphilis with areas of degeneration; endarteritis syphilitica of small cortical vessels, and late appearing dementia paralytica congenita.*

Clinical History.—E. G., a colored boy, aged 17, was admitted to the Philadelphia General Hospital, in the service of Dr. Edward Strecker, on June 5, 1928. He was a full term child, and no instruments were used at birth. The mother was colored, and the father Mexican. The patient walked and talked at the usual ages. He began school at the age of 5, and at 8 he developed what was called a "spastic condition of the right side of the body." He was able to walk, but "dragged" the right leg. After a month, use of the leg and face returned, while the arm improved only slightly. Following this he appeared better; he rode a bicycle, did roller skating, etc. In school he had difficulty in passing from one grade to another, so that at the age of 15 he had completed only the third grade. In school he was restless, and it was difficult to keep him in his seat like other children. He had always had a large head. There had been convulsive seizures from time to time during the past nine months; they were described as of grand mal character. During the past two years, since leaving school, he had shown progressive personality changes. He talked foolishly at times, laughed to himself and was very childish; he would rub the back of his head for varying lengths of time. During the past twelve months he had not been able to be up and about, except in a chair. The feet and legs appeared stiff, and he dragged both in attempting to walk. For the past three months he had been unable to speak. He lost control of the arms and was unable to feed himself. At no time did he complain of pain. Two weeks previous to admission, there was considerable contracture of the extremities.

The mother, aged 38, had always worked hard and was well. The father, aged 59, was reported as well. A sister died at the age of 10 months from marasmus. There was no history of miscarriages.

Examination.—The patient was markedly emaciated and underdeveloped, appearing to be about 9 or 10 years of age. The head was large and out of proportion to the rest of the body. The patient was mentally so markedly retarded that he could neither talk nor understand. He lay in bed on his back with the knees drawn up, and uttered a piercing cry at intervals. He did not attend to bodily wants. The eyes showed no muscle imbalance. The pupils were wide, irregular and absolutely fixed to light and in convergence. The reflexes were greatly exaggerated, especially on the left, where there were weakness and pyramidal tract signs.

Laboratory Analyses.—The Wassermann reaction of the blood was 4 plus. The spinal fluid contained 30 cells per cubic millimeter; there was an increase of globulin; the Wassermann reaction was 4 plus; the gold curve was 5555543310.

Course.—After admission, the mentality grew worse. The patient needed constant attention and had to be fed. He failed rapidly and died on June 21.

Brain Pathology.—Gross examination revealed intense leptomeningeal thickening and opacity anteriorly, which gave the brain an appearance as if milk had been poured over it. Frontal sections revealed marked internal hydrocephalus and an old area of softening in the left motor-parietal region, both cortical and subcortical.

Microscopically, the following features stood out: 1. There were intense leptomeningeal edema and fibrosis in the presence of a very moderate infiltration with round cells of the lymphocytic and plasma types, located particularly epicortically. 2. The cortex showed (fig. 7): (*a*) a mild disturbance of the architecture with a definite narrowing; (*b*) a marked prominence of the smaller vessels as a result

of the swelling and pyknosis of the nuclei of the endothelial and adventitial cells; (*c*) new vessel formation; (*d*) an intense increase in rod cells (Stäbchenzellen, Hortega cells); (*e*) a mild perivascular infiltration with both lymphocytes and plasma cells; (*f*) ganglion cell changes of all sorts from the mildest chromatolysis to the most severe degeneration; (*g*) a fairly marked increase of macroglia of fibrous type (fig. 8); (*h*) a definite increase of iron pigmentation; (*i*) only a slight increase of lipoid. 3. There was endarteritis of the Heubner type in the large blood vessels.

Anatomic Diagnosis.—The diagnosis was meningovascular syphilis, with areas of degeneration, endarteritis syphilitica of the small cortical vessels; dementia paralytica congenita.

Fig. 7 (case 5).—Section from a case of dementia paralytica congenita, toluidine blue stain, showing meningeal infiltration at *A*. A disturbance of the cortical architecture, endarteritis, and very mild perivascular infiltrations are seen.

Comment.—From the clinical standpoint, there can be no doubt that the syphilis was inherited. Jakob [2] has stressed that the hereditary form of dementia paralytica is characterized by the frequency of focal symptoms, many times of a subcortical nature, by marked vegetative disturbances, the more frequent finding of a frozen pupil, the occurrence of convulsions and cerebellar manifestations, a very slow course, with infrequent remissions, stunting of growth and peculiarities of the "biologic reactions."

In this case the history of mental deficiency from birth is clear, but definite mental symptoms did not occur until two years before death. There were focal symptoms of a subcortical nature in the form of a hemiplegia; an anatomic explanation for these can be found, first in the presence of syphilitic vessels, and second, in the old area of softening in the parietomotor cortex and subcortex. The question naturally arises whether this patient had had dementia paralytica from the beginning, or, as seems more reasonable, whether he did not have meningovascular

Fig. 8 (case 5).—Cajal preparation of the cortex, showing an intense macroglia overgrowth and an increase in blood vessels.

syphilis with the gradual development of a terminal dementia paralytic picture. That the latter possibility may be correct is evidenced by the cases described by Spatz [15] and Kufs.[7] This assumption would explain the clinical course better than would that of a dementia paralytic picture from the beginning.

Pathologically, the endarteritis of the small cortical vessels was prominent. Jakob [2] claimed that in juvenile dementia paralytica three

15. Spatz, H.: Zur Pathologie und Pathogenese der Hirnlues und der Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:644, 1926.

deviations from the usual dementia paralytic picture occur: 1. The frequent presence of true syphilitic changes in the brain, such as gumma, meningo-encephalitis, syphilitic changes in the large vessels and endarteritic manifestations in the small vessels. 2. Severe parenchymatous changes without marked inflammatory reaction. These are shown beautifully in our case. One could not make a diagnosis of dementia paralytica under the microscope from the presence of perivascular infiltrations. 3. Since Sträussler's [16] investigations, cerebellar changes have been stressed. These consist of numerous multinucleated Purkinje cells, a peculiar spindle-shaped dilatation of the axis cylinders and a severe tissue atrophy. In our case the cerebellum showed an occasional double nucleated Purkinje cell, but nothing else of note.

CASE 6.—*Abdominal pain for two days in a woman six months' pregnant. Frontal headache for several weeks, with swollen ankles and failing vision. Blood pressure high, with normal blood urea nitrogen, and moderate albuminuria; serology positive. Microscopic diagnosis: meningovascular syphilis with endarteritis of the small cortical vessels (syphilitic or toxic?).*

Clinical History.—R. T., a colored woman, aged 26, was admitted to the Philadelphia General Hospital, in the service of Dr. Catherine McFarlane, on Sept. 16, 1928. She was six months' pregnant. She complained of frontal headache for several weeks; abdominal cramps for two days, and swollen ankles for about two weeks. Vision had been failing, and lately she had been restless and nervous. The blood pressure was 220 systolic and 110 diastolic. There had been frequent attacks of bleeding from the nose and of subconjunctival hemorrhages.

Examination.—On admission the patient was restless and somewhat confused. The blood pressure was 224 systolic and 120 diastolic. There was albuminuric retinitis.

Course.—Five hundred cubic centimeters of blood was withdrawn from a vein; spinal puncture was done, and 50 cc. of clear fluid was withdrawn. Following this procedure, the blood pressure dropped to 200 systolic and 120 diastolic. Four days later, she stated that the headaches were much improved. On the following day general convulsive twitchings occurred, and gradually grew less frequent. The patient complained of suffocation, nausea and intense body heat. On the following day she became irrational; the pulse became weak, and the blood pressure dropped to 170 systolic and 100 diastolic. Dyspnea set in, and she died rather suddenly, on September 21.

Laboratory Examinations.—The specific gravity of the urine was 1.020; it contained considerable albumin, many hyaline casts, leukocytes and a few red cells. Examination of the blood showed: urea nitrogen, 15 mg. per hundred cubic centimeters; Wassermann reaction, 4 plus. The spinal fluid was normal.

Pathology of the Brain.—Grossly, there was nothing but an intense edema. Microscopically, the outstanding features were: 1. There was a mild infiltration

16. Sträussler, E.: Die histopathologischen Veränderungen des Kleinhirns bei der progressiven Paralyse, Jahrb. f. Psychiat. u. Neurol. **27:7**, 1906; Ueber Entwicklungstörungen im Zentralnervensystem bei der juvenilen progressiven Paralyse und die Beziehungen dieser Erkrankung zu den hereditären Erkrankungen des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **2:**20, 1910.

of the meninges (fig. 9 *A*) with round cells, mainly of the lymphocytic type, but with the presence of occasional plasma and phagocytic cells. This was by no means uniform, but was noted mainly at the base and deep in the fissures. 2. An occasional middle-sized vessel was to be seen in which Heubner endarteritis was present; this was shown particularly by a productive proliferation of the endothelium without degenerative changes. 3. In the cortex there was a marked endarteritis of the small vessels, in every way similar to that described by Nissl [17] and Alzheimer [18] as endarteritis syphilitica of the small cortical vessels; it was likewise exactly similar to that stressed by us in all sorts of toxic and infectious conditions.

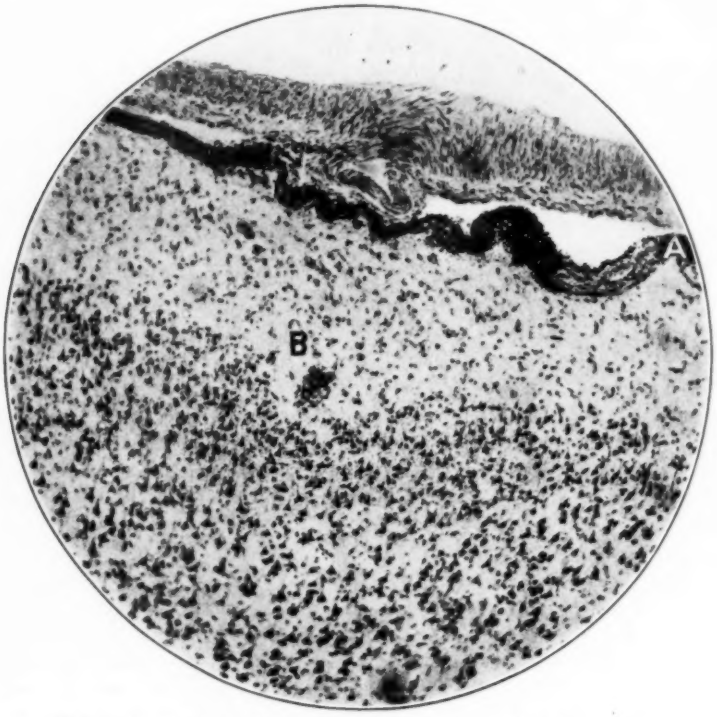

Fig. 9 (case 6).—Section from a case of meningeal syphilis.

So great was this proliferative change in the small vessels that in places the vessel walls were in apposition. Here and there one saw areas of incomplete softening ("Verödungsherde") and perivascular foci (fig. 9 *B*). 4. Throughout the cortex the ganglion cells showed fairly severe changes, not only of the ischemic type, but other degenerations as well. 5. Intense edema was present.

Microscopic Diagnosis.—The diagnosis was meningovascular syphilis, with endarteritis of the small cortical vessels (syphilitic, toxic or both).

17. Nissl: Zur Histopathologie der paralytischen Rindenerkrankungen, Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1904, vol. 1; Neurol. Centralbl. **23**:32, 1904.

18. Alzheimer, A.: Progressive Paralyse und endarteritische Hirnlues, Centralbl. f. Nervenh. **16**:443, 1905.

Comment.—From the clinical standpoint, this case presented signs and symptoms of a severe eclampsia; apart from a positive Wassermann reaction of the blood, it was in no way out of the ordinary. While syphilis is not usual in cases of this sort, this is by no means an isolated instance of the combination. From the pathologic angle, the severe endarteritis of the small vessels and small "Verödungsherde" in the cortex would have occasioned no surprise because they occur in many other cases of a toxic nature (Winkelman and Eckel,[19] Grinker and Stone[20]). However, the presence of definite evidences of syphilis in the brain was surprising. They consisted of a mild, yet definite, meningeal infiltration with lymphocytes and plasma cells, and an occasional vessel in which Heubner's endarteritic changes were to be seen. It is well known that endarteritis of the small cortical vessels may be the result of a syphilitic infection, as was demonstrated long ago by Nissl[17] and Alzheimer.[18] The question immediately arose as to the origin of the endarteritic changes in the small blood vessels in our case. Were they due to the toxemia of the eclamptic process, to syphilis or to both? In our previous articles on this subject we have stressed the absolute similarity of the toxic and syphilitic forms of endarteritis, so that it is impossible to distinguish them here.

CASE 7.—*Difficulty in walking, and within twenty-four hours incontinence and semistupor. Repeated serologic tests negative. Pathologic diagnosis: meningovascular syphilis.*

Clinical History.—F. S., a white man, aged 36, who was admitted to the Philadelphia General Hospital, in the service of Dr. C. W. Burr, on Aug. 2, 1927, complained that on the day before admission he did not feel well and in walking deviated to the right. On the following morning he could not get up from bed and was unable to talk. He was incontinent and semistuporous. No further history was secured.

Examination.—The patient was in a semistuporous state, from which he could be partially aroused; he was restless; at times he answered a few questions slowly; he was poorly oriented. The pupils were irregular and did not react to light or in accommodation. There was no nystagmus. The extra-ocular movements could not be tested. The eyegrounds were normal. There were no deformities and no edema of the limbs.

Course.—After two weeks in the hospital the condition grew worse. Weakness of both hands and arms developed. The muscles were held more or less rigid. There was slight weakness of both seventh nerves, while the other cranial nerves

19. Winkelman, N. W., and Eckel, J. L.: Productive Endarteritis of the Small Cortical Vessels in Severe Toxemias, Brain **50**:608, 1927; Endarteritis of the Small Cortical Vessels in Severe Infections and Toxemias, Arch. Neurol. & Psychiat. **21**:863 (April) 1929; The Brain in Bacterial Endocarditis, ibid. **23**:1161 (June) 1930.

20. Grinker, R. R., and Stone, T. T.: Acute Toxic Encephalitis in Childhood: A Clinicopathologic Study of Thirteen Cases, Arch. Neurol. & Psychiat. **20**:244 (Aug.) 1928.

were all normal. All tenden reflexes, in both the upper and the lower extremities, were active, especially on the left. An Oppenheim sign was present on the left, but the Babinski sign was indefinite. There was ankle clonus on the left. The patient picked up objects with difficulty, apparently because of muscular weakness. Sensation could not be tested. At this time the eyegrounds showed prominent veins, and the disks were slightly blurred. The retinas were edematous. The ears were normal.

During the last two weeks in the hospital the temperature ranged from 100 to 103 F. The pulse rate ranged from 120 to 160; the respiratory rate, from 30 to 40. The condition became rapidly toxic. There were marked attacks of sweating and

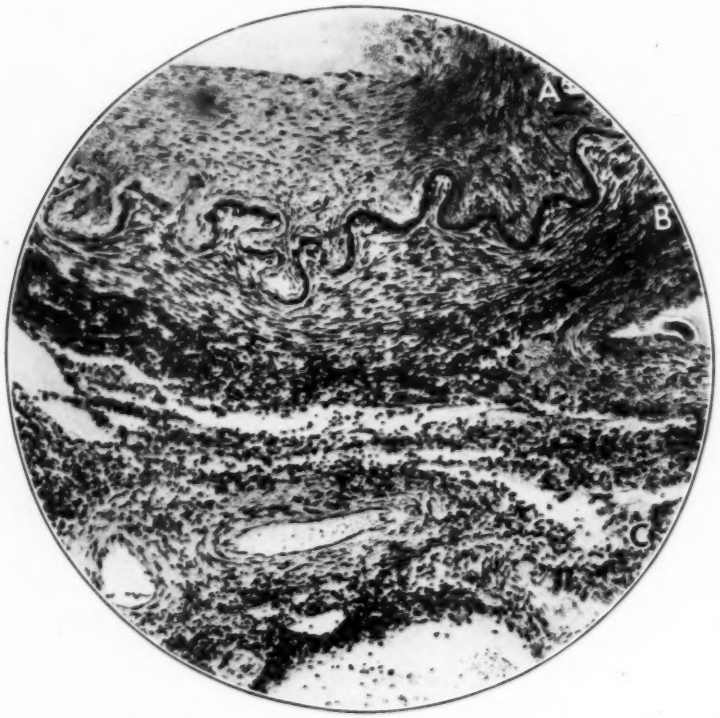

Fig. 10 (case 7).—Section from a case of meningovascular syphilis; toluidine blue stain, showing a marked Heubner type of endarteritis with tremendously proliferated intima, without degenerative changes (*A*), marked adventitial infiltration with plasma cells (*B*) and meningeal infiltration (*C*).

slight rigidity of the neck. There was a bilateral Kernig sign, and the muscles were held rigid. The eyes deviated to the left. The weakness continued, and the patient died on September 29.

Laboratory Examinations.—Examination of the blood showed: hemoglobin, 18.3 Gm.; red cells, 6,140,000; white cells, 13,700; Wassermann reaction, made several times with Kolmer and cholesterol-fortified antigens, always negative; sugar, 90 mg.; urea nitrogen, 14 mg. Several taps of spinal fluid revealed from 4 to 6 cells per cubic millimeter; a very faint trace of globulin; a negative Wassermann reaction, and a gold curve of 1222100000.

Pathologic Examination.—Gross examination of the brain disclosed marked leptomeningeal thickening, especially at the base, where it reached a thickness of nearly 0.5 cm. On cross-section through the pons the thickened meninges were whitish and almost cartilaginous in consistency.

Microscopic examination showed a low grade meningeal inflammation throughout the entire nervous system, with fibrosis and the presence of infiltrating cells of both lymphocytic and plasma types. Over the anterior surface of the pons there were the following changes: 1. The basilar vessels (fig. 10) showed a marked proliferative endarteritis without degenerative changes. The elastic lamina was unaltered. The adventitia showed thickening and infiltration with lymphocytes and plasma cells. The medium-sized vessels also showed the Heubner type of change. 2. The pia-arachnoid was involved in an intense edema and fibrosis, in which were numerous lymphocytes and plasma cells, especially the latter (fig. 10 *C*). No invasion of the pontile tissue was noted. 3. The fifth nerve root in relation to the pons showed a marked infiltration with the same type of inflammatory cells as those within the subarachnoid space.

Diagnosis.—The diagnosis was meningovascular syphilis. (Somewhat similar cases have been described by Malamud,[21] Löwenberg [22] and von Robustow.[23])

Comment.—From the clinical standpoint, the most important feature was the completely negative serology. The question is often asked "Does syphilis of the nervous system occur with completely negative serology"? Cases of this kind are not common, but they do occur (Kafka,[24] Schmidt-Kraepelin,[25] von Robustow, Kufs). They do not, however, occur with sufficient frequency to justify the general procedure of some neurologists in treating all patients with antisyphilitic remedies in the presence of negative serology. In the entire collection of material in this laboratory, aside from old cases of tabes, there are not six cases of this sort. It is well recognized, of course, that in long-standing tabes negative serology is not unusual, but the ordinary meningovascular syphilis usually gives a positive reaction either in the blood or in the spinal fluid.

In this case, during the course of the disease in the hospital the eyegrounds showed the beginning of a choking of the disks. Conditions causing an increase in intracranial pressure, such as a brain tumor, were considered, and clinically the case did suggest a brain tumor.

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21. Malamud, W.: Zur Klinik und Histopathologie der chronischen Gefässlues in Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:778, 1926.

22. Löwenberg, K: Zur Klinik und Histopathologie der chronischen Syphilis der Hirngefässe, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:799, 1926.

23. von Robustow: Klinische und histopathologische Beiträge aus dem Gebiete der chronischen Syphilis des Zentralnervensystems, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:757, 1926.

24. Kafka, V.: Atypische serologische Befunde bei Paralyse und ihre Bedeutung, Ztschr. f. d. ges. Neurol. u. Psychiat. **56**:260, 1920.

25. Schmidt-Kraepelin, T.: Beiträge zur Kenntnis der serologischen und anatomischen Befunde bei Paralysen mit langsamen Verlauf, Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:144, 1926.

COMMENT

We have described seven cases of unusual types of syphilitic involvement of the central nervous system. Three were gross gummas, one in the brain, one in the pons and one in the cord. It is common experience that large syphilitic granulomas are now extremely rare. This may be because treatment is instituted earlier and is more energetic. However, there has been such a dispute about the occurrence of miliary gummas. Jakob [2] thought that they are relatively frequent in malignant types of syphilis, especially in dementia paralytica, while Spielmeyer [26] denied their frequent occurrence. While gummas may occur within the parenchyma, in all three of our cases they were in relation with the meninges. This recalls the theory of Spatz, who believed that in dementia paralytica the organism reaches the brain through the blood stream, while in cerebral syphilis it goes by way of the spinal fluid. While theoretically this holds in cases such as we have described, Jakob has expressed certain objections to the theory of Spatz. It does not explain the more marked involvement of the frontal lobes in dementia paralytica, nor the relative sparing of the pallidum even when its neighbor, the putamen, is severely affected.

Intramedullary gummas of the cord are extremely rare, just as are intramedullary tuberculomas and metastatic lesions, but all of these lesions are more common in relation to the meninges. This is probably to be explained by the fact that the anterior and posterior spinal arteries are not in the line of the direct blood flow from the vertebral vessels; metastatic particles consequently are carried upward into the basilar vessel.

We have described also a case of juvenile dementia paralytica with severe endarteritis of the small cortical vessels and a large area of softening. This patient had convulsions, and the case belongs in the group that Alzheimer has called the epileptic form of endarteritic brain syphilis. In this case we have explained the pathologic picture as did Kufs [7] in a similar case. We believe that this patient suffered originally from congenital hydrocephalus with cerebral syphilis, and that eventually a dementia paralytic process was added. This case would further substantiate the ideas that Spatz has expressed. However, the combination of cerebral syphilis and dementia paralytica is extremely uncommon.

We have included also a case of multiple small areas of softening throughout the spinal cord. This has been called by Henneberg "pure vascular spinal syphilis." In these cases there have been numerous individual vascular insults in the spinal cord, similar in every way to those seen in pseudobulbar brain lesions. This really represents a new

26. Spielmeyer, W.: Zur Frage der Häufigkeit und Bedeutung miliärer Gummen bei Paralyse, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:320, 1926.

syndrome, described for the first time in 1920 by Henneberg. The symptoms in his case correspond in practically every detail with those we have described. Henneberg's patient was a man, aged 46, with a history of attacks of "rheumatism." He had had a syphilitic infection. He had iritis, bladder and bowel incontinence and weakness of the legs, which later approached a flaccid palsy, with eventually absence of reflexes but with a positive Babinski sign. All forms of sensations were decreased in the lower limbs. He had girdle paresthesias about the abdomen. Decubitus and toxemia developed, and the patient died. Multiple small areas of softening were found throughout the entire cord substance in the distribution of the small vessels.

Strangely enough this is one of the two cases in our series with negative serology. The other case with negative laboratory studies was one of a severe meningovascular syphilis in which the pathologic picture was extremely characteristic.

In one case we have described a meningovascular syphilitic picture along with an endarteritis of the small vessels which may have been due either to a toxic process, to syphilis itself or to both.

SUMMARY AND CONCLUSIONS

1. Seven unusual cases of syphilitic involvement of the central nervous system are reported.

2. Three cases of gumma are included. In all the process began as a focal meningitis with secondary invasion of the parenchyma.

3. Cerebral syphilis and dementia paralytica may be combined in the same case, as in our case that terminated as juvenile dementia paralytica.

4. Negative serology was present in two cases, both of the vascular type, one of the brain and one of the cord.

5. Cerebral syphilis and a toxemia of any sort may produce severe cortical endarteritic changes in the small blood vessels which are indistinguishable from one another.

ABSTRACT OF DISCUSSION

Dr. Joseph H. Globus, New York: The observations made by the investigators must stand as they are presented, unless one takes the trouble to go over the material carefully; I do not question the ability of the investigators to present the evidence correctly. Hence their observations must be accepted. The value of the presentation lies mainly in the fact that additional cases of syphilis, which deviate somewhat from the type familiar to every one of us, have been presented, and it reopens an old discussion of syphilis of the central nervous system which has for some years been neglected. I think that is the value of the presentation, particularly now that many new therapeutic measures are employed in the treatment for syphilis, such as malaria, and various claims are made for regressive alterations in the brain without a clear understanding of their relation to atypical forms. In

order more correctly to evaluate some of the findings in autopsy material after new therapeutic measures have been employed, one must become familiar with atypical forms of syphilis.

Dr. Israel Strauss, New York: In the cases with a negative serology was there a history of a chancre?

Dr. N. W. Winkelman: No.

Dr. Strauss: It is true, as Dr. Winkelman says, that today one rarely sees gummas clinically, and that this is due probably to the effect of the rather intensive treatment practiced today; however, it seems to me that cases of this kind are a reflection on the medical profession for permitting cases to progress without sufficient treatment, even though there may be a negative Wassermann reaction. The criticism does not apply only to the medical profession, but also to the ignorance of the layman in regard to the seriousness of this disease. This reverts to the physician, however, in that in instructing the lay public he fails to instil into their minds what syphilis is and what it can do. Unquestionably, instruction of soldiers in the service during the World War had an excellent effect on public opinion, but I do not think that we have gone far enough. I wonder why neurologists, who see and are acquainted with the extreme ravages of this disease, take such a passive attitude, when in tuberculosis and cancer there is active propagandism, which is reaping results that are unquestionably of great value. It is true that psychiatrists have been acting along these lines. Of course, in dealing with syphilis one must meet a certain attitude of mind which considers that the disease is to be treated or spoken of askance and in a subdued voice, but I think that the medical profession should take an active part in curing ignorance of this kind; then, cases of this type, rare though they are, would probably not occur.

Dr. Bernard Sachs, New York: There are a few points of historic interest that might be mentioned in connection with this discussion. I wish to remind Dr. Strauss that gummas always have been rare, since long before the period of improved antisyphilitic treatment; in fact, I think that among all tumors that occur in the brain the gummas are probably as rare as any, so that I do not think one can attribute this fact to either improved or nonimproved methods of treatment.

I have also been interested in the fact that after all, in the last twenty to twenty-five years, the differentiation, for instance, between syphilis and tuberculosis has evidently not progressed; taking it now as here presented, although there are no distinguishing characteristics of the syphilitic process, particularly in the central nervous system, other than the meningovascular process and the specific endarteritis, everything else would seem to be an extremely indifferent sort of factor and one must fall back on the only two definite evidences of the syphilitic processes that were available more than twenty years ago.

One point that Dr. Globus made I had in mind, and I think that it should lead to further pathologic studies. There is no doubt, particularly with the modern malarial treatment and with intensive treatment with various metallic substances, that the pathologic processes should at least show some differences from those that were described twenty years ago. After all, what are seen in most of these cases are terminal stages of the syphilitic processes. It seems to me that what one should seek in the future is the evidence of retrogressive changes, so that one can really have evidences of what the methods of treatment are accomplishing.

Dr. William G. Spiller, Philadelphia: I agree with what Dr. Sachs has said. For many years, until the laboratory for neuropathology was established at the Philadelphia General Hospital, of which Dr. Winkelman has charge, I received

much of the pathologic material from neurologic cases in that hospital and for a long time taught the students of the University of Pennsylvania that gumma is one of the rarer tumors of the brain.

Dr. Winkelman has remarked that in a certain number of the cases that he has studied the laboratory findings regarding syphilis were negative. I was a chief in the service of that hospital for twenty-five years, and frequently I began my lectures with a series on tabes. I was at first surprised at the reports that in many of these old, long-standing, undoubted cases of tabes the laboratory findings were entirely negative for syphilis.

Dr. J. B. Ayer, Boston: By saying that the tests were negative, does that include cytology and everything?

Dr. Winkelman: Yes.

Dr. Ayer: One would think, in the last case particularly, in which I think that you said the serology was negative, that if the fluid had been drained, in the last half you might have found a number of cells. The meninges appeared to be loaded with lymphocytes. I have noticed that this method has a certain value, the so-called fractional examination employed in such cases. I was wondering if it had been employed here.

Dr. N. W. Winkelman, Philadelphia: To Dr. Sachs' question as to whether anything has been added to the older methods of distinction between a syphiloma and a tuberculoma, I think that the silver fibril stain which I showed, the Klarfeld preparation, is one of the most important distinguishing features. Tuberculosis is a destructive disease, while syphilis is a proliferative disease. It is true, as Dr. Sachs and Dr. Spiller have said, that the final opinion between tuberculosis and syphilis is the finding of the specific organism. In my own experience the presence of giant cells is more common in syphilitic than in tuberculous lesions. That is supposedly against the ordinary pathologic teaching. The presence of plasma cells is about equal in both. So that, aside from the two points of destruction and proliferation and the specific organism, I do not believe that much has been added to the differential diagnosis.

There is one thing that has struck me forcibly as the result of treatment. Many times there is a complete disappearance of the acute inflammatory manifestations. One then finds the Heubner type of endarteritis without the inflammatory evidence. Treatment does take away the inflammation in these cases in the same way that it does the inflammation in dementia paralytica. We have not included cases of that sort because they are fairly common.

As to Dr. Ayer's question about the spinal fluid results, the finding of a slight increase of globulin might be taken as evidence of an abnormal spinal fluid, but I do not believe that one could say that an increase of globulin and a small increase of cells, say 15 or 20, would be in favor of syphilis in the absence of a positive Wassermann reaction and the absence of a change in the colloidal gold curve; that is what we mean when we say that the spinal fluid was essentially normal.

Regarding Dr. Strauss' question about the history of an initial lesion, I think that a good many of the patients at the Philadelphia General Hospital, when they are able to give a history, are fairly honest and tell of the initial lesion some twenty, thirty or forty years before; we have obtained, in most of these cases, a much higher percentage of histories of an initial lesion than in private practice.

CHRONIC PROGRESSIVE CHOREA

THE PATHOGENESIS AND MECHANISM; A HISTOPATHOLOGIC STUDY *

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The mechanism of the production of choreo-athetotic movements, in spite of careful and thorough histopathologic studies, is still inadequately explained. It is believed by some that choreic movements can be explained solely by disease of the ganglion cells or fiber system of the striatum. S. A. K. Wilson [1] was of the opinion that the "problem of all involuntary movements, as tic, epilepsy, tremor, chorea, athetosis, myoclonus, etc., is one of physiology" and not of pathology. It was his contention that the "choreic disturbance manifests itself through the cortico-spinal system." The latter must be in a relatively intact condition for the appearance of hyperkinetic symptoms. For eleven years he had had under observation a patient with senile chorea in whom the choreic movements were limited to the right side of the body. Pathologically, the left postcentral convolution was shrunken to nearly half its size, while the entire left corpus striatum appeared normal. In Wilson's opinion these findings are sufficient to explode the striatal theory of chorea. He considered the atrophy of the left postcentral convolution of great significance and offered the hypothesis that for the occurrence of choreic movements it is necessary to have a relatively integral efferent (corticospinal) tract. He also pointed out a number of clinical facts that would indicate that in cases of choreo-athetosis

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* From the Neuropathological Laboratory and Neurological Division, Montefiore Hospital.

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1. Wilson, S. A. K.: Die Pathogenese der unwillkürlichen Bewegung mit besonderer Berücksichtigung der Chorea, Deutsche Ztschr. f. Nervenh. **107**:28, 1929; Disorders of Motility and Muscle Tone with Special Reference to the Corpus Striatum: IV. Involuntary Movements and Their Pathogenesis; Chorea and Athetosis, Modern Problems in Neurology, New York, William Wood & Company, 1929, p. 209; Lancet **2**:1 (July 4); 53 (July 11); 169 (July 25); 215 (Aug. 1); 268 (Aug. 8) 1925.

the afferent tracts from the cerebellum via the subthalamic region to the thalamus and the brain cortex are also involved. If these pathways are thrown out of action completely by disease, the involuntary movements cease. This is well shown in Magnus'[2] experiments on decerebrate rigidity, in which choreic movements do not occur. S. A. K. Wilson further pointed out that choreic patients are unable to influence voluntarily the movements or to bring them to a standstill. Physiologically, he suggested that this can be explained only by the changes in the postcentral region found in his case. He concluded that chorea and choreoathetosis represent a complex type of involuntary movements for the production of which a motor mechanism having its seat in the cortex is required. A defect in the afferent cerebellomesencephalothalamocortical regulation produces these involuntary movements. No theory that assigns a single destructive lesion in the corpus striatum as the cause of chorea will adequately explain the facts. Mingazzini and Wimmer (at a meeting of the German Neurological Society in 1928) expressed views that tended to support S. A. K. Wilson's hypothesis.

We have had the opportunity of studying three cases of chorea. In doing so we have considered the views of S. A. K. Wilson and others. We have also tried to reconcile our findings and the views of these observers with the occasional absence of choreo-athetotic movements in diseases of the neostriatum occurring in the course of degenerative, inflammatory, arteriosclerotic and neoplastic diseases. It will be unnecessary to recapitulate and reevaluate the classic histopathologic studies of chorea; the reader is referred to the contributions of Alzheimer,[3] Jelgersma,[4] C. and O. Vogt,[5] Hunt,[6] Jakob,[7] Dunlap[8] and others.

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2. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

3. Alzheimer, A.: Ueber die anatomische Grundlage der Huntingtonschen Chorea und der choreatischen Bewegungen überhaupt, Autoreferat, Ztschr. f. d. ges. Neurol. u. Psychiat. **3**:566, 1911.

4. Jelgersma, G.: Neue anatomische Befunde bei Paralysis agitans und bei chronische Chorea, Neurol. Centralbl. **27**:995, 1908.

5. Vogt, C., and Vogt, O.: Zur Lehre der Erkrankungen des striären Systems, J. f. Psychol. u. Neurol. **25**:3, 1920. Vogt, C.: Quelques considérations générales à propos du syndrome du corps striée, J. f. Psychol. u. Neurol., Ergänzungshefte **18**:479, 1911-1912.

6. Hunt, J. R.: Progressive Atrophy of the Globus Pallidus, Brain **40**:58, 1917.

7. Jakob, A.: Die extrapyramidalen Erkrankungen, in Foerster, O., and Willmanns, K.: Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1923, vol. 37, p. 42.

8. Dunlap, C. B.: Pathologic Changes in Huntington's Chorea, Arch. Neurol. & Psychiat. **18**:867 (Dec.) 1927.

REPORT OF CASES

CASE 1.—*History.*—B. N., a woman, aged 35, married, was admitted to the Montefiore Hospital on Sept. 13, 1925. In August, 1922, she had begun to feel nervous and irritable. She fell occasionally and dropped objects from her hands. In February, 1923, there was a fire in her house from which she escaped by jumping from the roof across to the neighboring one. Shortly after this exciting incident, there appeared unsteadiness in gait and involuntary movements of all extremities. One brother was known to have had a classic case of Huntington's chorea. Most of the members of her family were constitutional psychopaths and were frequent offenders against the law.

Physical Examination.—The results of examination of all the organs, except the nervous system, were negative on admission.

Neurologic Examination.—There were generalized choreiform movements which were aggravated by emotional factors and voluntary acts. Accompanying the chorea were athetotic and dystonic fragments. There were ptosis of the left eyelid and irregularity of the pupils. The right pupil was larger than the left and reacted sluggishly to light. The deep reflexes were hyperactive, and there was a questionable bilateral Babinski sign. The mental status of the patient was normal on admission.

Laboratory Data.—On admission the results were negative. In 1929, the patient developed a severe secondary anemia. Examination of the blood showed: hemoglobin, 22 per cent; red cells, 2,400,000; total and differential white cell counts were normal. Two days before death, the hemoglobin dropped to 10 per cent and the red cells to 1,600,000; the appearance of the red cells was characteristic of secondary anemia. The blood pressure was 120 systolic and 50 diastolic. All other laboratory tests gave negative results.

Course.—The patient's condition remained unchanged until March, 1929, when she complained of dizziness and weakness. She showed generalized wasting, marked pallor and evidence of severe secondary anemia. The chorea and other neurologic signs remained unchanged. Except for slight euphoria there were no psychic disturbances. In March, 1930, she had a temperature of 100 F.; she died on March 21, 1930, seven and a half years after the onset of the illness.

Clinical and Anatomic Diagnosis.—The diagnosis was Huntington's chorea, secondary anemia (cause undetermined), cardiac dilatation and chronic passive congestion of the viscera.

Autopsy Report.—Gross Examination: The brain was small, weighed 1,000 Gm., and was markedly anemic. The frontal lobes were atrophic, more so on the left; the fissures between the frontal gyri were widely separated, and the pia-arachnoid was adherent over the left frontal convolutions. The brain was sectioned coronally. There were moderate symmetrical hydrocephalus, narrowing of the cortical gray matter and shrinkage of the basal ganglia, affecting primarily the neostriatum (caudate and putamen) (fig. 1). The spinal cord, except for an anemic appearance, presented no abnormalities.

Microscopic Examination: Complete coronal sections through the basal ganglia and small sections from the various cortical areas, cerebellum, brain stem and spinal cord were stained by the myelin sheath (Weil modification), hematoxylin-eosin, cresyl violet and Mallory phosphotungstic acid methods. Frozen sections from the same regions were stained by the Cajal gold sublimate (Globus modification), Bielschowsky, del Rio Hortega (Penfield modification) and Victoria blue methods.

Cortex: In the complete coronal sections through the frontal convolutions, the cortex was shrunken. The tips of the anterior horns of the lateral ventricles were dilated (fig. 1). The centrum ovale (with the myelin sheath stain) presented a slight lacunar appearance without demyelinization of the fibers. The white matter appeared considerably reduced. The pia-arachnoid was thickened owing to a proliferation of the arachnoidal cells.

Frontal Lobes: With the cresyl violet stain, sections through convolutions F_1, F_2 and F_3 showed a distortion in the arrangement of the cyto-architectural layers (fig. 2*A*). Throughout these layers, particularly in the third and fifth laminae, there were minute circumscribed foci of destruction (Verödungsherde) and a decrease in the number of the nerve cells (fig. 2*B*). These ganglion cells exhibited various changes, such as simple loss of Nissl substance, shrinkage and

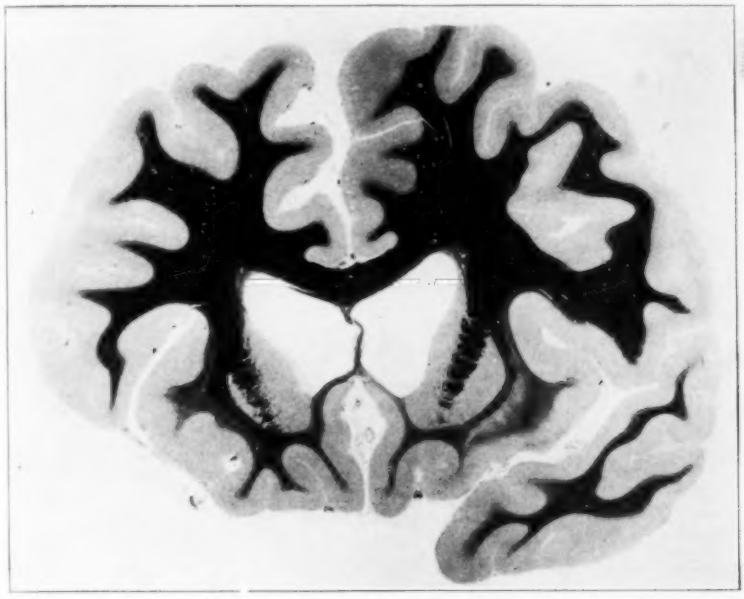

Fig. 1.—Coronal section through the rostral end of the neostriatum, showing shrinkage of the caudate and putamen and a dilatation of the anterior horns of the lateral ventricles. Myelin sheath stain (Weil modification).

pyknosis. Some of the nerve cells in the foci of destruction were completely disintegrated. The increased glial reaction in the white matter consisted of protoplasmic astrocytes. The blood vessels were not affected.

Similar changes were found in the precentral (fig. 2*B*), postcentral and temporal convolutions. In the precentral gyri, the large ganglion cells suffered less destruction than the small ganglion cells. All other convolutions were fairly well preserved.

Basal Ganglia: Sections through the basal ganglia, with the myelin sheath stain, showed a moderate dilatation of the lateral and third ventricles. The caudate and putamen were shrunken, especially on the right (figs. 1 and 3). The globus pallidus at the caudal end also appeared shrunken (fig. 3*B*). The neostriatum and right globus pallidus were in a lacunar state. Most of these lacunae, in the

Mallory phosphotungstic acid sections, were lined by a layer of endothelial cells and a wall of glia fibers. The gliosis was most intense in the anterior third of the caudate and putamen. Throughout these gray nuclear masses were small scattered necrobiotic foci. The left pallidum appeared pale and was poor in its content of myelinated fibers. In the cresyl violet sections many of the nerve cells of the caudate and putamen showed extensive pathologic changes, which were more marked in the rostral end. The small ganglion cells suffered more than the large cells. In some sections the former were completely absent and were replaced by glia nuclei. The majority of the small cells were poor in chromatin and appeared

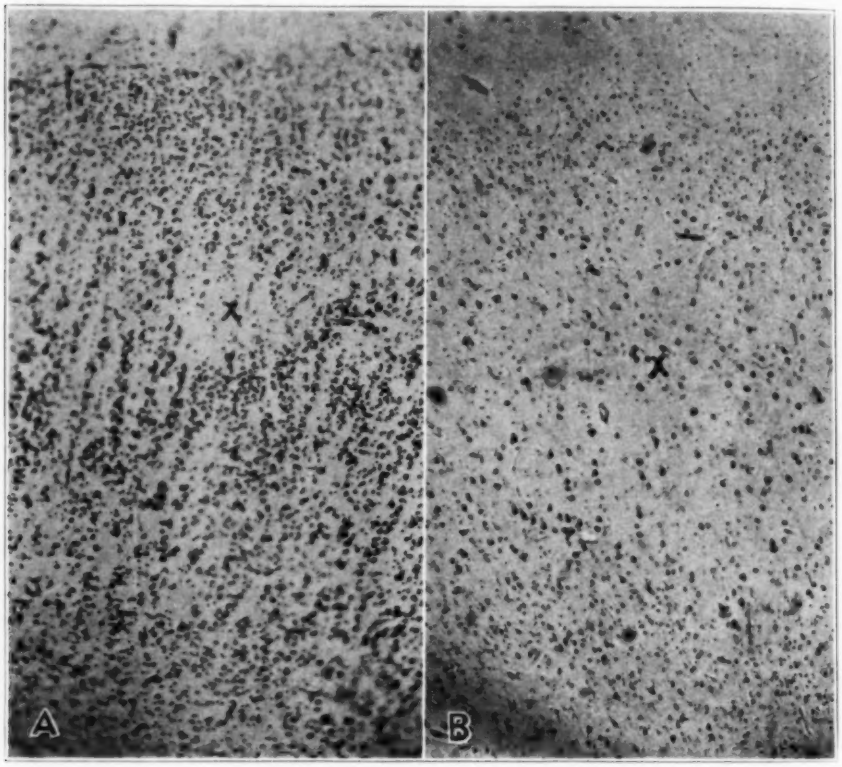

Fig. 2.—*A*, the section from the frontal lobes, showing distortion in the architectural arrangement of the cortical layers, a decrease in the ganglion cells and an area of destruction (*x*). *B*, a section from the motor area, showing the same process with a decrease in the ganglion cells in the third and fifth layers. At *x* is an area of destruction (Verödungsherd). Cresyl violet stain; × 40.

shrunken; they had lost most of their cytoplasm and could be identified only by their nuclei (figs. 4 and 5). Some of the large ganglion cells stained more deeply than normally and were shrunken; others had undergone chromatolysis. The shrunken area, poor in nerve cells, was rich in protoplasmic astrocytes in which fat droplets were occasionally found. The blood vessels, except for enlarged perivascular spaces in which products of degeneration (fat) were found, showed

nothing of note. The changes in the pallidum were not quite as characteristic as those in the neostriatum. The right globus pallidus was smaller than the left (fig. 3*B*). The ganglion cells stood out prominently and were well preserved, except for occasional cells that were shrunken and pyknotic. There was an increase in the glia nuclei. The ganglion cells of the amygdaloid nucleus presented degenerative changes somewhat similar to those in the caudate and putamen.

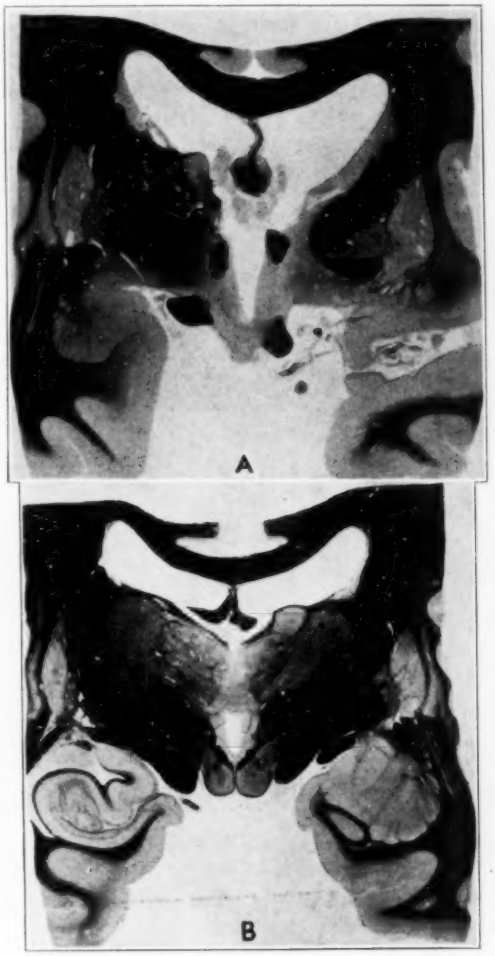

Fig. 3.—*A*, a coronal section through the middle of the basal ganglion, showing shrinkage of the caudate, a lacunar state of the putamina and a dilated ventricular system. *B*, a coronal section through the caudal end of the basal ganglia, showing shrinkage of the right putamen and globus pallidum. Myelin sheath stain (Weil modification); reduced from a magnification of × 2.

Thalamus and Subthalamic Region: The lateral nucleus of the right thalamus had a slight lacunar appearance. Most of the nerve cells of the thalamic nuclei were well preserved. The corpora luysii, tuber cinereum, mammillary bodies, sub-

stantia innominata of Reichert and substantia nigra appeared normal. The ependyma of the lateral and third ventricles was thickened and had numerous verrucae.

Cerebellum: Sections of the cerebellum in various regions showed scattered foci of destruction in the granular layers (Verödungsherde) (fig. 6), characterized by an extensive loss of the cells, which were replaced mostly by microglia. The Purkinje cells bordering these foci remained fairly intact. The pons and medulla oblongata showed no changes.

The spinal cord, except for a slight paling of the spinocerebellar pathways, showed nothing of note.

Microscopic Diagnosis.—The diagnosis was chronic degenerative chorea (Huntington).

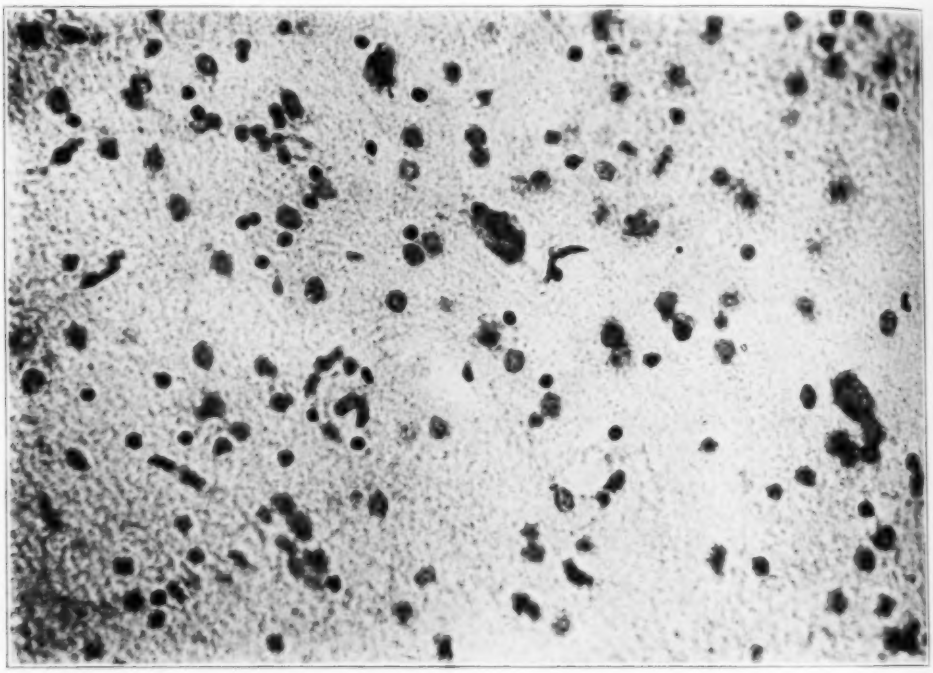

Fig. 4.—Section from the caudate nucleus, showing a decrease in the number of small ganglion cells. Those present can only be identified by their nuclei. Two of the large ganglion cells did not show marked pathologic changes. Cresyl violet stain; reduced from a magnification of × 480.

Comment.—This case presented some unusual features. The patient suffered from a severe secondary anemia, which was the ultimate cause of death. In this respect our case is somewhat similar to case 4 of Jakob, in which the blood picture resembled that seen in pernicious anemia; the patient died of cachexia. Our patient was free from mental symptoms during the seven and a half years of illness. It is mere

speculation to say that if she had lived longer she might have developed a psychosis such as is observed in Huntington's chorea.

Histopathologically, there was involvement of the cortex from the frontal to the postcentral gyri, affecting primarily the third and fifth layers. The neostriatum, especially at its rostral end, was shrunken and contained nerve cells undergoing various stages of degeneration; the small ganglion cells were more extensively involved than the large cells. There was also slight involvement of the right globus pallidus, both amygdaloid nuclei and the granular layers of the cerebellum. These

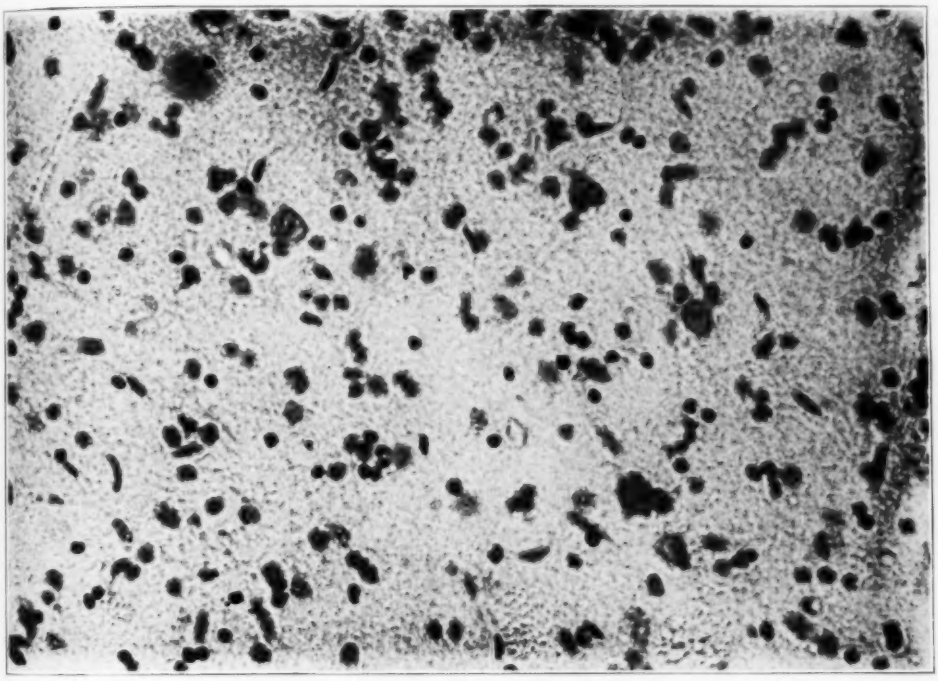

Fig. 5.—Section from the putamen, showing poorly stained small ganglion cells and destruction of a few of the large ganglion cells. Cresyl violet stain; reduced from a magnification of × 480.

pathologic changes, except for those in the cerebellum, conform somewhat to those described by Jakob and Dunlap.

Case 2.—*History.*—T. B., a man, aged 62, was admitted to the Montefiore Hospital on Aug. 15, 1922. In 1920, his gait had become unsteady, resembling that of a drunkard. Soon thereafter, involuntary movements developed which involved first the lower extremities and later spread to the face, trunk and upper extremities. The dyskinesia was aggravated by mental or emotional strain, and was less pronounced when the patient was at rest. In May, 1922, bulbar signs, such as hoarseness, paroxysmal cough and nasal regurgitation developed. When 25 years

of age he had had a chancre, for which he received antisyphilitic treatment. Except for the fact that he subsequently developed ulcers over both tibiae, there were no symptoms to indicate active syphilitic infection after the primary lesion. The family history was significant in that his mother had had peculiar involuntary movements of the extremities which appeared late in life (after the age of 70). She died at the age of 77. Accurate information regarding these movements was not obtained.

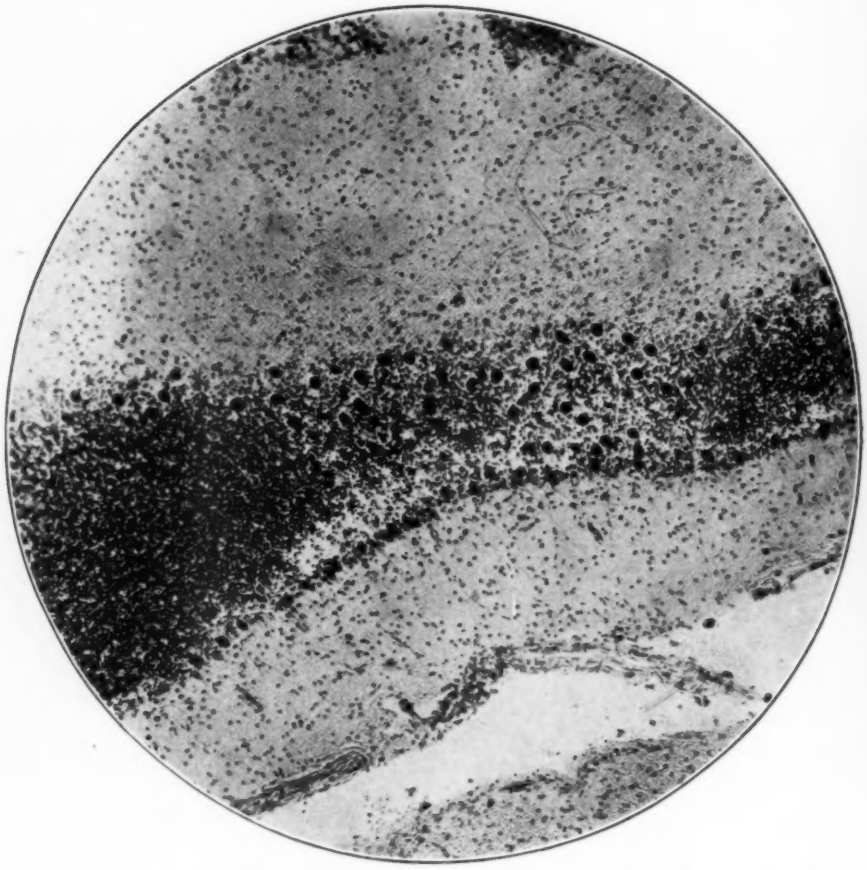

Fig. 6.—Section from the cerebellum, an area of rarefaction in the granular layer. Cresyl violet stain; × 50.

Physical Examination.—The patient was emaciated and cachectic, and presented signs of bilateral pulmonary tuberculosis, laryngeal tuberculosis and healed ulcers over both tibiae.

Neurologic Examination.—The gait was ataxic with a tendency toward right lateropulsion. The head was tilted to the right. There were coarse, jerky, vermicular movements of all the extremities, with suggestive athetosis of the fingers, twisting movements of the trunk, facial grimacing, blinking of the eyelids

and tremor. There was ptosis of the right eyelid; the right pupil was larger than the left, and both reacted sluggishly to light. All the deep reflexes were hyperactive; the abdominal reflexes were absent, but there was no Babinski sign. Sensory examination, except for slight impairment in position sense in the toes, gave negative results.

Mental Examination.—The patient was euphoric and distractible. His speech was rambling. He was disoriented, and his memory was poor for recent and remote events.

Laboratory Data.—A roentgenogram of the chest revealed extensive bilateral pulmonary tuberculosis. The sputum contained tubercle bacilli. An examination of the blood showed: red cells, 3,800,000; white cells, 3,200; differential count,

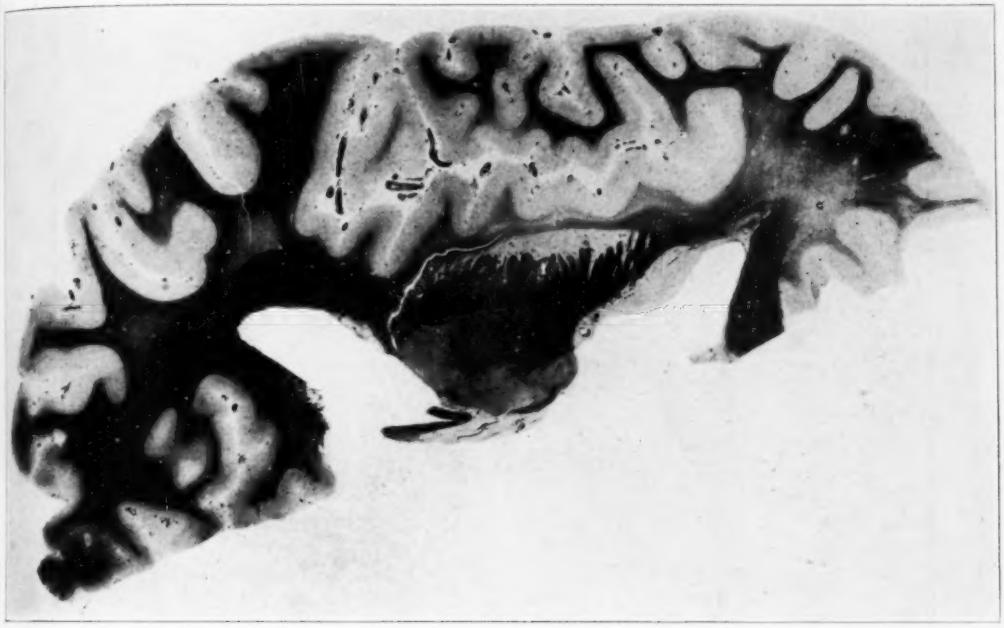

Fig. 7.—Horizontal section through the basal ganglia, showing demyelinization of the fibers in the frontal and parietal regions. The fibers of the posterior two thirds of the internal capsule stained poorly when compared with those of the anterior limb. Myelin sheath stain (Weil modification); × 1.

normal. The urine showed a heavy trace of albumin, many leukocytes and occasional granular casts. The blood pressure was 100 systolic and 75 diastolic.

Course.—In the hospital the patient had a fever of between 99 and 102 F. He died of a terminal bronchopneumonia on Aug. 31, 1922, about two years after the onset of the dyskinesia.

Clinical and Anatomic Diagnosis.—The diagnosis was Huntington's chorea, chronic pulmonary tuberculosis, tuberculosis of the larynx, tuberculous ulcerations of the ileum and cecum, miliary tubercles of the liver and spleen and bronchopneumonia.

Necropsy.—Gross Examination: The brain weighed 1,250 Gm. The pia was thickened and adherent to the cortex. Over the cerebellum and frontal regions there was a small amount of sanguineous fluid. The frontal gyri were atrophic, and the fissures were widely separated. The vessels at the base were slightly thickened. The right hemisphere was cut horizontally, and the left was cut vertically. The lateral ventricles were dilated. The left caudate and putamen were somewhat smaller than normal.

Microscopic Examination: Sections of the brain were stained by the same methods as in case 1. With the myelin sheath stain there was partial demyeliniza-

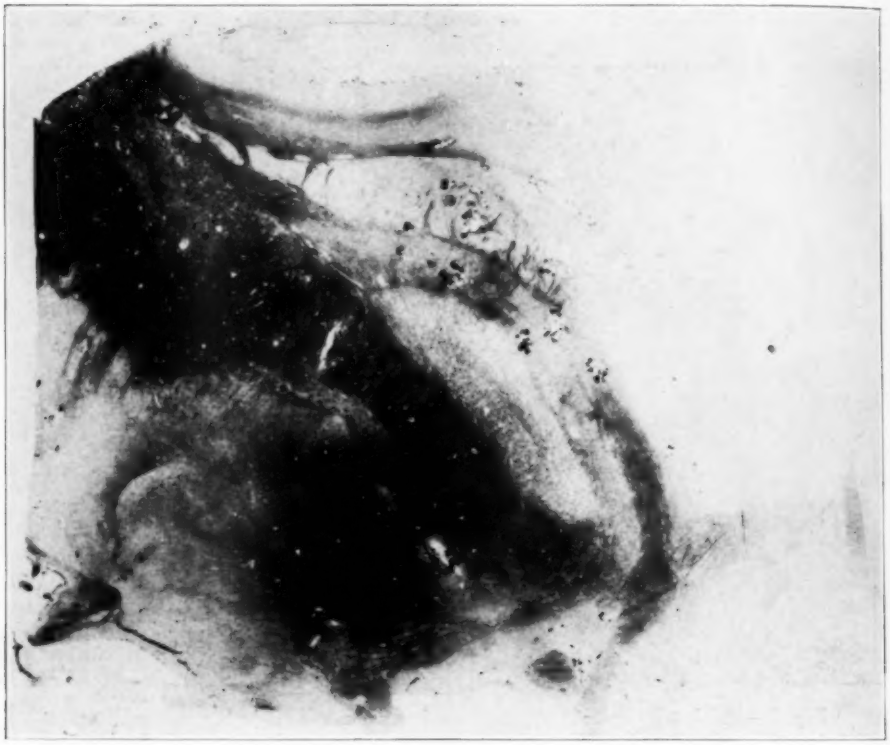

Fig. 8.—Section through the caudate, putamen and globus pallidum, showing shrinkage and a lacunar state with deposition of iron pigment. Myelin sheath stain (Weil modification); × 2.

tion of the centrum ovale near the frontal and temporal lobes (fig. 7). The right caudate and putamen were not shrunken, but contained numerous grapelike bodies (Buscaini). Similar grapelike bodies were also present in the internal capsule and in the striae nuclei of the left hemisphere. The pia-arachnoid was thickened in places, the result of proliferation of arachnoidal cells and pigment accumulation.

Cortex: In the frontal lobes, with the myelin sheath stain, there was a slight demyelinization of the white fibers. Swelling and disintegration of some of these fibers were seen under a higher magnification. The arrangement of the architectural layers of the cortex through convolutions F_1, F_2 and F_3 was fairly well pre-

served. In the third, fifth and sixth laminae the ganglion cells were decreased, stained rather poorly and showed pathologic changes in the acute and chronic stages. There was a definite increase in the capillaries, and a few of the vessels showed atherosclerotic changes, with a tendency toward obliterative endarteritis. Sections from the precentral and postcentral gyri showed changes similar to those in the frontal region; the third lamina was most involved. Sections from the occipital lobe showed a lacunar state of the white fibers.

Basal Ganglia: In the myelin sheath sections, the left putamen and globus pallidus were slightly shrunken (fig. 8). The putamen, the first segments of the

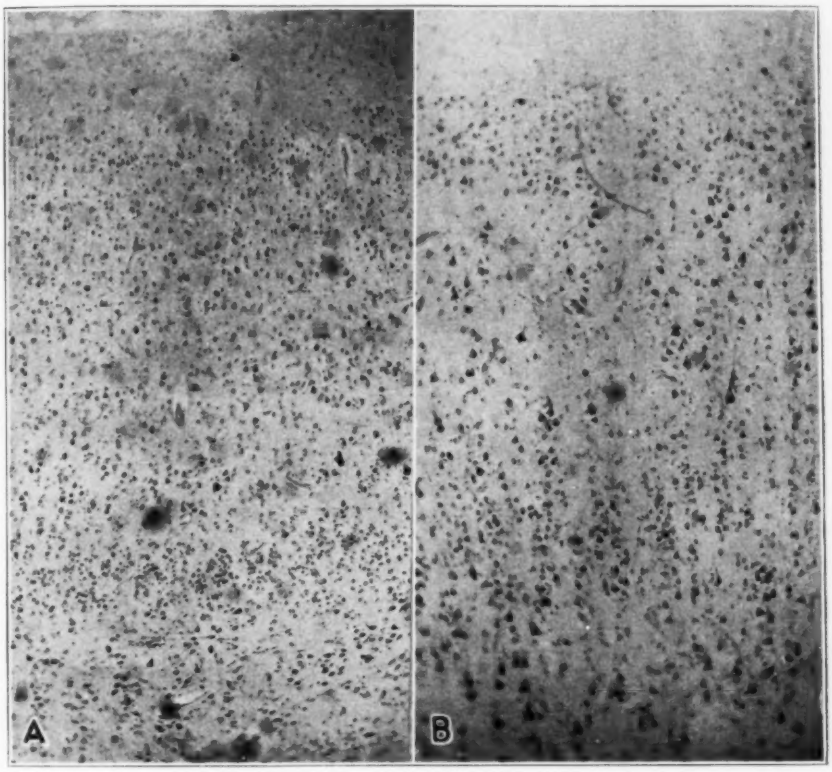

Fig. 9.—*A*, section from the frontal lobes, showing scantiness of nerve cells in the third layer and shrinkage of the fifth and sixth laminae. *B*, section from the motor cortex, showing a slight distortion in the architectural arrangement of the cortical layers and an outfall of ganglion cells in the third cortical layer. Cresyl violet stain; × 40.

globus pallidus and the internal capsule had a lacunar appearance (fig. 8). Under a higher magnification, in the cresyl violet sections, some of the small ganglion cells of the upper third of the caudate and putamen showed pathologic changes, such as swelling, eccentrically placed nuclei, loss of chromatin substance, pigment atrophy and occasionally complete destruction. The large ganglion cells were much less affected. Some of the lacunar spaces were surrounded by a ring of glia

cells. Deposits of iron pigment around the lacunar spaces were a conspicuous feature (fig. 8). Buscaini bodies were also present as shown in figure 7. The changes in the basal ganglia were less pronounced than those found in the first and third cases. The thalamic nuclei, corpora luysii, paraventricular nuclei, substantiae nigrae and the red nuclei did not show any pathologic changes. The pons, apart from having a lacunar appearance, was normal.

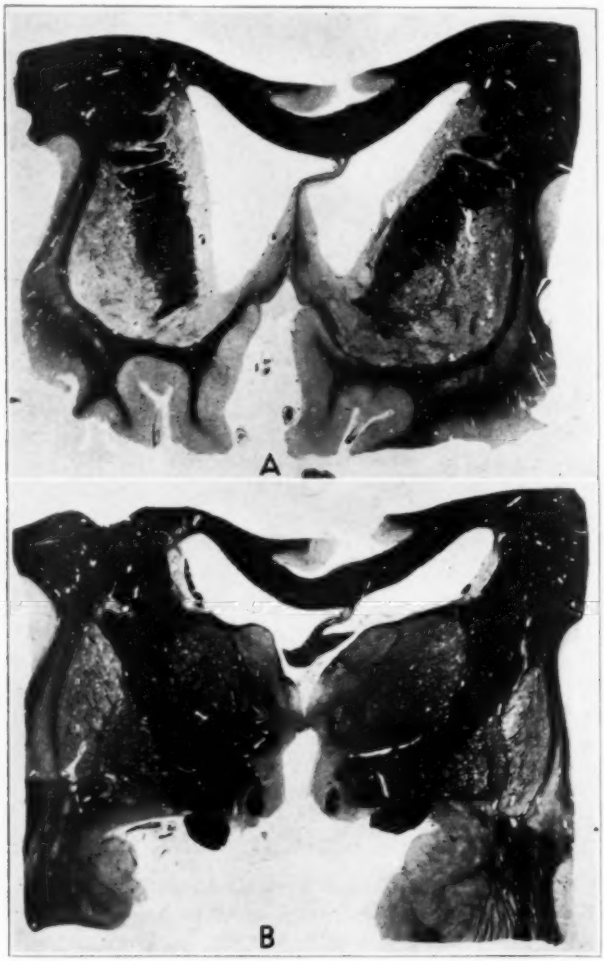

Fig. 10.—*A*, a coronal section through the anterior third of the neostriatum, showing a markedly shrunken caudate, a slightly shrunken putamen, a lacunar state of both of these and enlarged anterior horns of the lateral ventricles. *B*, a coronal section through the middle half of the striatum, showing shrinkage and a cribriform state of the neostriatum (putamen and caudate) and a marked cribriform state of the globus pallidus. Myelin sheath stain (Weil modification).

The cerebellum was normal. The spinal cord was not secured at autopsy.

Microscopic Diagnosis.—The diagnosis was chronic degenerative chorea.

Comment.—Clinically, the patient presented typical choreiform movements and mental deterioration. Since the hereditary factor is questionable, it is doubtful whether this case belongs to the Huntington group. The changes in the nervous system in this case were mild when compared with the first and third cases. The arrangement of the cortical layers was well preserved. There were excessive proliferation

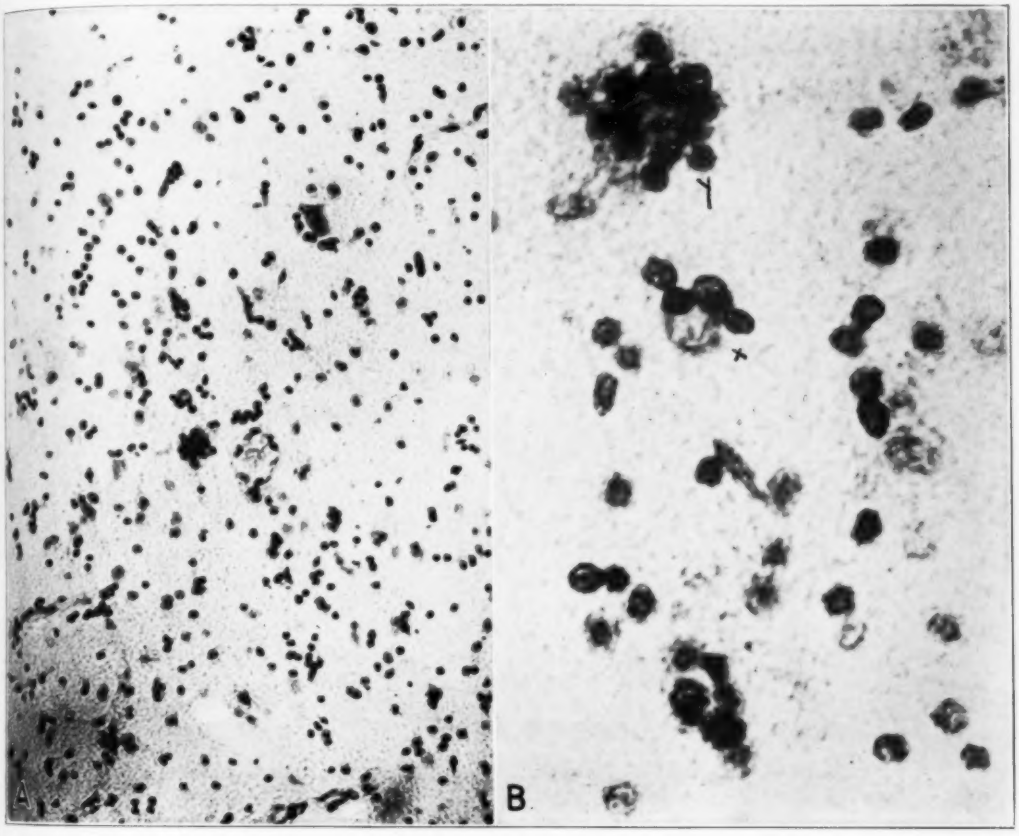

Fig. 11.—*A*, section through the left caudate nucleus, showing poorly stained small ganglion cells, scantiness of the same and neuronophagia of some of the large ganglion cells; reduced from a magnification of × 240. *B*, same as *A*, showing destruction of the small ganglion cells (*x*) and neuronophagia of one of the larger ganglion cells (*y*). Cresyl violet stain; reduced from a magnification of × 960.

of the capillaries and moderate atherosclerosis of the vessels. There were pathologic changes of the ganglion cells in the third, fifth and sixth layers of the frontal lobe and the postcentral gyri. The small nerve cells of the neostriatum showed marked pathologic changes; the large cells were less severely affected. The unusual histopathologic finding

in this case was the demyelinization of the white fibers of the frontal, parietal and temporal lobes.

CASE 3.—*History.*—E. T., a widow, aged 54, who was admitted to the Montefiore Hospital on July 7, 1925, had been well until July, 1924, when for some unknown reason she fell and lacerated her scalp. She did not lose consciousness and showed no evidence of intracranial injury. Soon afterward, involuntary movements of the extremities, head and neck developed. During the first year of the illness she lost about 50 pounds (22.7 Kg.). The previous history was without significance. As far as could be ascertained, no other members of the family had had chorea or any other disorder of the nervous system.

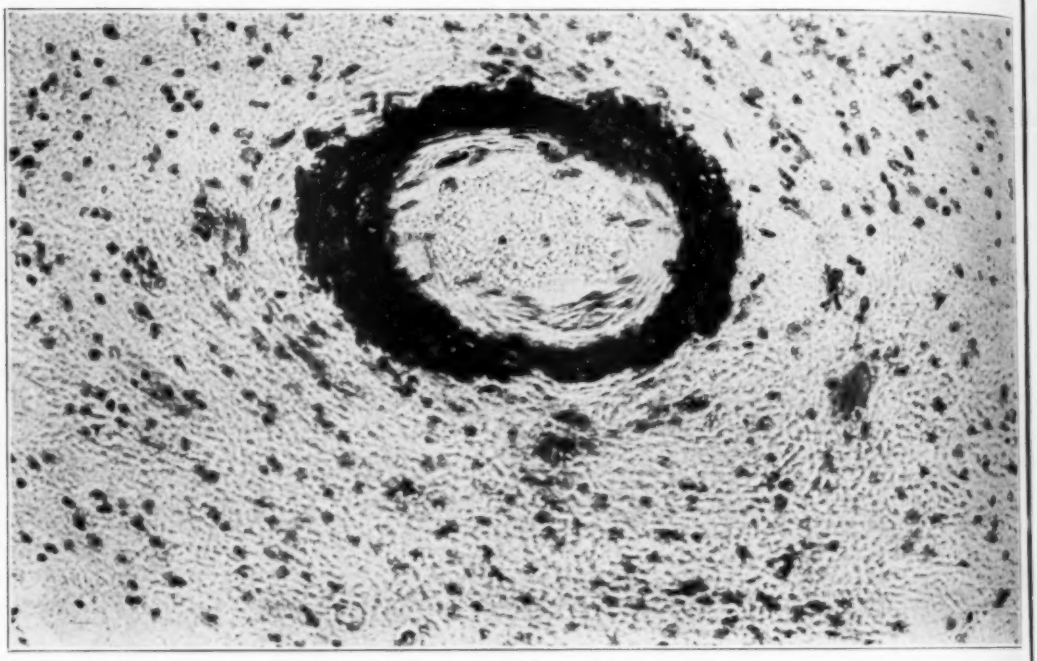

Fig. 12.—Calcification of the media and adventitia in a vessel of the putamen. Cresyl violet stain; × 240.

Neurologic Examination.—There were generalized choreiform movements of all muscles of the body, with a dystonic fragment in the left foot. The left pupil was larger than the right, but both reacted to all stimuli. There were hypotonia of all the extremities, rebound phenomena and dysdiadokokinesia in both upper extremities. The patient showed mental symptoms, such as impairment of memory, disorientation as to time and place and poor insight into her condition.

Laboratory Data.—All laboratory tests gave negative results.

Course.—The involuntary movements remained unchanged. The mental condition, however, became worse, the patient developing hallucinations and delusions of persecution. In June, 1930, an abscess developed on the right thigh, which was incised and drained. The condition ran a febrile course, and there developed a rigid

neck and a Babinski sign on the left. The patient died on June 27, 1930, about four years after the onset of the chorea.

Clinical and Anatomic Diagnosis.—The diagnosis was chronic degenerative chorea (arteriosclerotic), generalized arteriosclerosis (slight), abscess of the right thigh and parenchymatous degeneration of the viscera.

Autopsy Report.—Gross Examination: The brain weighed 1,000 Gm. All convolutions, especially the frontal, were markedly atrophic, and the fissures from the frontal to the postcentral convolutions were widely separated. The vessels at the base of the brain showed atherosclerotic changes. The pia-arachnoid was thickened and adherent to the gray matter. The brain was cut coronally in the antero-

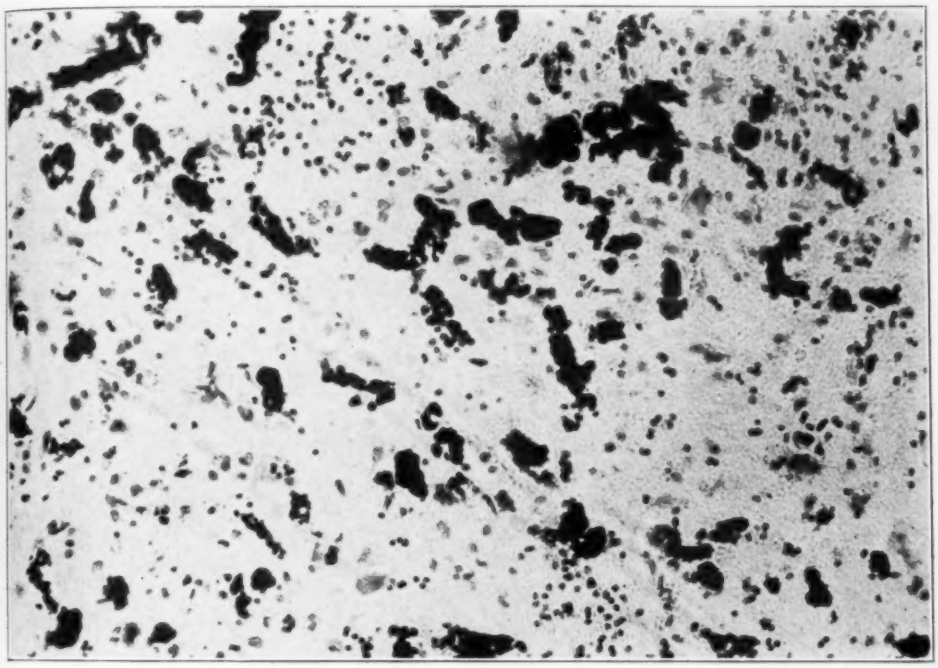

Fig. 13.—Section from the right putamen, showing numerous calcified bodies. Some of these were calcified capillaries. Cresyl violet stain; reduced from a magnification of × 240.

posterior direction. There was a uniform enlargement of the lateral ventricles, which was more marked in the anterior horns.

The meninges of the spinal cord showed numerous scaly plaques over the lumbar and sacral regions. The cervical and thoracic cord were thinned out, and some of the segments were constricted. When the cord was cut, areas of apparent translucency were seen in the white matter.

Microscopic Examination: Complete coronal and small celloidin and frozen sections were studied by the same methods as in the previous two cases.

Cortex: In the frontal lobes, with the myelin sheath stain, sections through convolutions F_1, F_2 and F_3 showed shrinkage of the cortical layers and the white

matter, with a lacunar state of the latter. The white fibers were not demyelinated. In the cresyl violet sections the cortical layers could be distinguished, but were narrower than normal (fig. 9*A*). The nerve cells within most of the layers, especially the fifth and sixth, were decreased and showed chromatolytic changes, shrinkage and pyknosis. Occasional swelling and vacuolation were also observed. There were no foci of destruction (Verödungsherde) such as were seen in cases 1 and 2. The glia cells (microglia and protoplasmic astrocytes) were increased in number. There were no evidences of inflammatory reactions. The pia-arachnoid was thickened in places. The vessels of the white matter showed moderate atherosclerotic changes. Occasional perivascular infiltration by glia cells was also noted. Several of the vessels of the white matter showed calcification of the media; in a

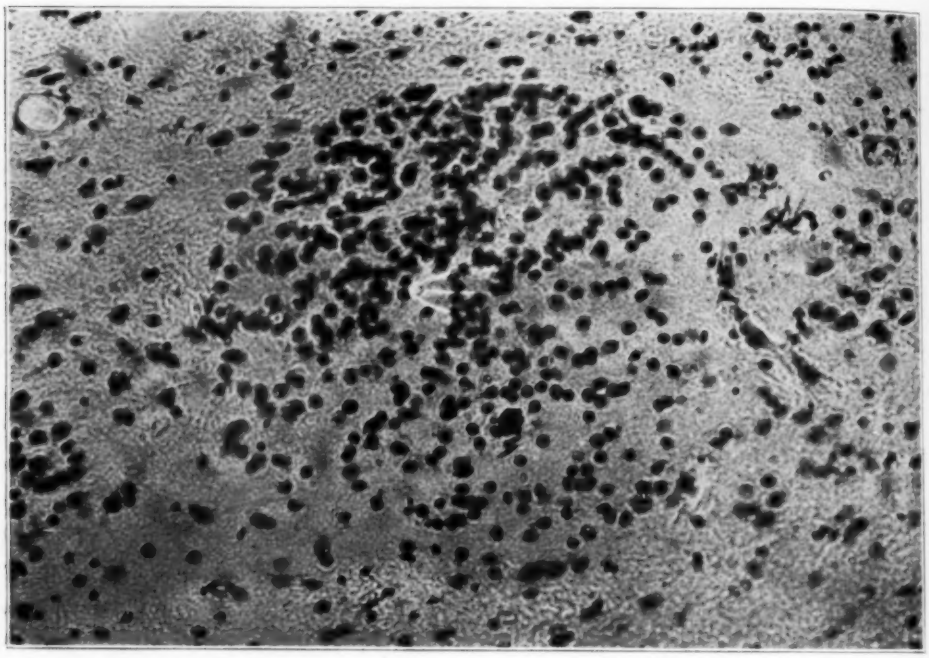

Fig. 14.—A collection of glia cells in the putamen. Cresyl violet stain; × 100.

few there was calcification of all the coats with complete obliteration of the lumina. A few corpora amylacea were found within the white and gray matter. In spite of the atherosclerotic changes of the vessels in the white matter, there were no changes such as have been described by Spielmeyer under the designation of "functional circulatory interference."

The precentral and postcentral gyri showed slight distortion in the architectural arrangement of the cortical layers (fig. 9*B*). There were also small foci of destruction (Verödungsherde) in which the nerve cells were completely destroyed. The giant pyramid cells of Betz appeared fairly well preserved, although the smaller ganglion cells showed the same changes as those in the frontal region. Sections in the parietal region showed one sector of the cortex to be paler than the rest, with marked destruction of the nerve cells. This resembled the changes

arising from the so-called functional vascular disturbances described by Spielmeyer. The vessel changes and the glia reaction were somewhat similar to those observed in the frontal regions. Sections from the temporal, hippocampal and occipital regions did not show any marked changes.

Sections through the neostriatum showed a markedly shrunken caudate, a slightly shrunken putamen, a cribriform state of the neostriatum and paleostriatum and enlarged anterior horns of the lateral ventricles (fig. 10). The white fibers of the centrum ovale were well preserved. The rostral and lateral part of the right caudate showed an accumulation of calcified bodies, which were found in the vicinity of the smaller capillaries. The vessels showed marked atherosclerotic changes and were surrounded by areas of gliosis. The nerve cells, especially the small ganglion

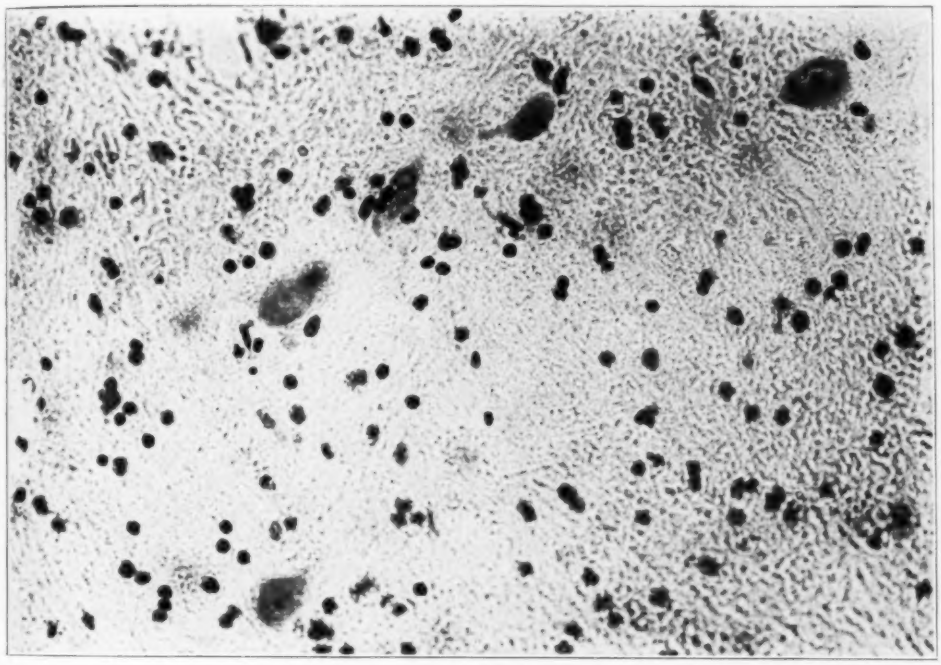

Fig. 15.—Section from the right globus pallidum, showing scantiness, the poor staining quality of the pigment and atrophy of the ganglion cells. Cresyl violet stain; × 480. Reduced from a magnification of × 480.

cells, were decreased in number, poor in chromatin, shrunken and had poorly stained nuclei (fig. 11). These changes were less marked than those in case 1. The larger ganglion cells, except for occasional neuronophagia (fig. 11 *B*), were fairly well preserved. In the left caudate the same changes were encountered as in the right. There was an increase in the number of proliferated capillaries, and some of the vessels showed calcification of the media (fig. 12). The amyloid bodies seen in the right caudate were absent here. The right putamen was loaded with calcified bodies (fig. 13). The vessels showed marked atherosclerotic changes, and some of the capillaries were completely calcified, their lumina being obliterated. The changes in the small ganglion cells were the same as in the

caudate; some of the large ganglion cells showed pigment atrophy. Occasional foci of destruction were also observed. In places, nodules of glia cells were found (fig. 14). There was an increase in the microglia and protoplasmic astrocytes similar to that observed in the caudate. Similar changes were found in the left putamen.

The changes in the globus pallidus resembled those in the neostratum; i. e., thickened and calcified vessels, corpora amylacea, increase in glia nuclei, and occa-

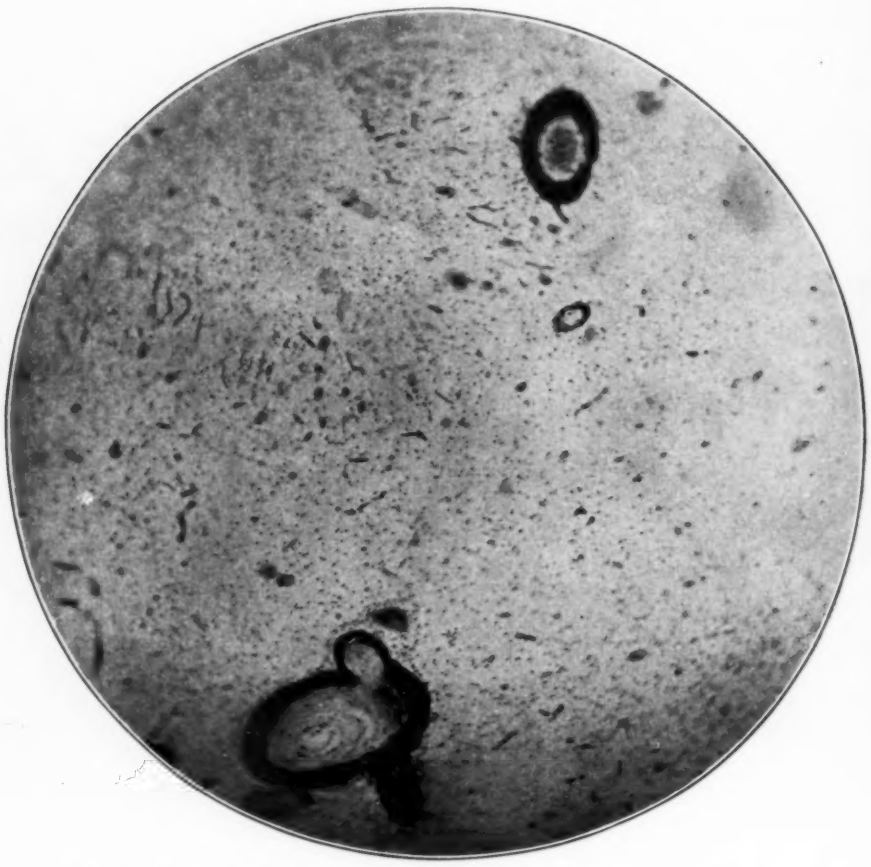

Fig. 16.—Two calcified vessels in the folia of the white matter, near the dentate nucleus. Cresyl violet stain; × 50.

sional destruction and pigmentation of the ganglion cells, which were diminished in number (fig. 15). The thalamic nuclei, tubera cinerea, corpora luysii, mammillary bodies, red nuclei, substantiae nigrae and pons, except for an occasional calcified vessel and the presence of amyloid bodies, did not show any marked changes.

Sections of the cerebellum in the region of the dentate nucleus showed a slight paling of the white fibers. With a higher power, a few of the myelin sheaths were seen to be fragmented. Within the white matter there were many calcified vessels

(fig. 16) and numerous corpora amylacea. The granular layers were studded with calcified bodies, some of which were calcified capillaries (fig. 17). The Purkinje cells stained poorly and were shrunken and atrophic; some Purkinje cells were completely destroyed. The nerve cells of the dentate nucleus stained poorly; some of the cells were shrunken, and others appeared swollen and had eccentrically placed nuclei. Calcified vessels were also found in this area.

Fig. 17.—Calcified bodies within the granular layer of the cerebellum. Cresyl violet stain; × 50.

The medulla oblongata, in the region of the tenth and twelfth cranial nerve nuclei, showed that the nerve cells of the reticular substance were smaller and contained little Nissl substance. The nuclei were often eccentrically placed, and there was frequent pigment atrophy. The vertebral artery showed marked atherosclerotic changes. The choroid plexus contained numerous psammoma bodies, more than those seen normally. Sections of the medulla oblongata in the region of the crossed pyramidal tracts showed a distortion of the ventral portion. Misplaced areas of gray matter gave the lower part of the medulla oblongata a heterotopic

appearance. The region of the ventrocerebellar pathways was occupied by gray matter. The central canal was dilated. The nerve cells, except for those in the pseudoheterotopic areas, were well preserved. There were no evidences of inflammation.

In the cervical region of the spinal cord, where the cord was constricted, the myelin sheath stain revealed destruction of the gray matter and of the ventral pathways. The anterior horn cells stained poorly and were decreased in number. The gray and white matter were studded with numerous calcified plaques. The meninges were slightly thickened, and the meningeal vessels, especially those of the posterior surface, showed atherosclerotic changes.

Microscopic Diagnosis.—The diagnosis was chronic chorea, arteriosclerotic.

Comment.—Clinically, the patient in case 3 presented a classic picture of chorea and some cerebellar signs. Pathologically, arteriosclerotic changes were scattered throughout the cerebrospinal axis. The most extensive involvement occurred in the caudate, putamen, globus pallidus and cerebellum. In the latter, the pathologic process was confined chiefly to the dentate nucleus. The cortex presented arteriosclerotic changes from the frontal to the precentral areas. The preponderance of involvement was in the fifth and sixth laminae, the third layer being fairly well preserved.

GENERAL COMMENT

Grossly, all three cases showed convolutional atrophy extending from the frontal to the central gyri. There was a moderate internal hydrocephalus in cases 1 and 2. The caudate and putamen were shrunken in cases 1 and 3; the shrinkage was confined to the globus pallidus in case 2. Microscopically, the ganglion cells of the cortex showed changes of the acute and chronic stages, with the preponderance of involvement in the third, fifth and sixth cortical laminae. In case 3, the third cortical layer was less affected than the corresponding layer in the first two cases. The same changes were present in the small ganglion cells of the neostriatum and to a lesser extent in the large cells; the pallidal cells were moderately involved by the same process. The granular layers of the cerebellum were affected in cases 1 and 3. In case 3, in which the pathologic changes were most widespread, owing to the calcification of the vessels, the involvement included the dentate nucleus and the substantia reticularis. Of importance in case 2 were the demyelinization of the white fibers in the region of the frontal and temporal lobes and the moderate atherosclerotic changes of the vessels.

When these findings are compared with the large series described by Jakob and Dunlap, it is readily observed that in essence the pathologic changes were alike, except that we found marked changes in the third cortical laminae in the first two cases and changes in the cerebellum in cases 1 and 3. Dunlap found the cerebellum involved in only one of his seventeen cases. In contrast to Dunlap's cases, but in conformity

with Jakob's, we found that the rostral portions of the striatum were more involved than the caudal.

What is the significance, if any, of these pathologic observations? What relationship do they bear to the views expressed by S. A. K. Wilson, who opposed the striatal theory. The choreic and athetotic manifestations in cases without evidence of striatal involvement cannot be dismissed lightly. Such cases were also observed by Horsley,[9] who succeeded in checking persistent athetosis in an upper extremity by excision of the corresponding motor cortex, and by Minkowsky,[10] Littmann,[11] and Lafora,[12] who brought forth additional pathologic and experimental evidence rejecting the striatal theory. Lafora produced choreo-athetoid movements in cats by lesions of the cerebellar peduncles, red nucleus and hypothalamic region. Lotmar [13] was also of the opinion that choreic movements may be caused by lesions of the cerebellum, anterior cerebellar peduncles, red nucleus, corpus luysii, thalamus or the corpus striatum.

The frequent observations of neostriatal lesions without choreo-athetotic manifestations should deter one from accepting the striatal theory as the sole explanation of these involuntary movements. The cortical changes described by most observers in chorea, involving chiefly the frontal gyri, as well as the occasional lesions found in the cerebellum and other regions, should lead one to consider these structures as important in this mechanism. On the basis of fairly constant neostriatal changes in choreo-athetosis we are loath to accept the view that the striatum does not play any rôle in this mechanism. We prefer to accept the views expressed by S. A. K. Wilson in 1924, when he stated that:

> The relation of the corpus striatum to the rest of the motor system is one of tone control and of control of innervation. Remove its influence by disease and cerebello-mesencephalo-spinal motor mechanisms come into overaction in spite of the normal activity of the pyramidal system; in fact, a universal muscular rigidity appears distinct from the selective rigidity of cortico-spinal disease; or alternately, involuntary movements develop, over which the control of the motor system, the cortico-spinal, is at best fleeting and imperfect.

9. Horsley, V.: The Function of the So-Called Motor Area of the Brain, Brit. M. J. **2**:125, 1909.

10. Minkowsky, M.: Experimentelle und anatomische Untersuchungen zur Lehre von der Athetose, Ztschr. f. d. ges. Neurol. u. Psychiat. **102**:650, 1926.

11. Littmann, J.: Experimenteller Beitrag zur Lehre von der Athetose, Schweiz. Arch. f. Neurol. u. Psychiat. **21**:1, 1927.

12. Lafora, G. R.: Chorea y athetosis experimental, Siglo méd. **70**:463, 1922.

13. Lotmar, F.: Die Stammganglien und die extrapyramidal-motorischen Syndrome, in Foerster, O., and Willmanns, K.: Monographien aus dem Gesamtgebiete der Neurologie und Psychiatrie, Berlin, Julius Springer, 1926, no. 48.

It is exactly the removal of this influence of the neostriatum by disease that permits the appearance of the involuntary movement. Without pathologic changes in this organ we wonder how frequently chorea would be manifested. The frequent cortical and subcortical changes in these cases, as well as the striatal changes, force us to admit the complexity of the factors in the production of this dyskinesia. The choreo-athetosis cannot be attributed to single lesions, and we must agree partly with S. A. K. Wilson that interference with the cerebello-mesencephalothalamocortical system is of importance in the production of these movements.

SUMMARY AND CONCLUSIONS

Three cases of chronic progressive chorea are presented: one of Huntington's type, one of questionable Huntington's type and one arteriosclerotic.

Histopathologically, all showed cortical and neostriatal changes. Cases 1 and 3 also showed cerebellar changes.

An attempt was made to interpret the mechanism of chorea on a corticostriatal basis.

ABSTRACT OF DISCUSSION

DR. N. W. WINKELMAN, Philadelphia: I was very much gratified to hear Dr. Davison state that not only the small cells of the striatum but also the large cells were involved. I believe that there is no distinction between the two in the striatum. There is no embryologic relation between the cells of the pallidum and the large cells of the striatum. The large and small cells of the striatum, however, are developed from the same embryologic structures.

It has been our finding that calcification of the vessels of the pallidum and of the striatum is a fairly frequent finding in cases in which there are no symptoms referable to these organs.

DR. CHARLES DAVISON: As regards Dr. Winkelman's discussion, I think I have emphasized that the calcifications of these vessels were found throughout the entire nervous system. They were less numerous in the cerebral hemispheres than in the striatum and cerebellum. I have shown a section of the cerebellum and dentate nucleus in which calcified vessels and amyloid bodies were found. I am familiar with the view of Hatfield and others, that calcified vessels are found in the globus pallidum of normal persons. I am more of the opinion expressed by Hallvorden and Spatz, that the condition is a pathologic exaggeration of a possible normal condition in both the globus pallidus and the substantia nigra.

Abstracts from Current Literature

THE NERVOUS MECHANISM OF ASSOCIATED EYE MOVEMENTS (ANDREAS HÖGYES). DANIEL KUHLMANN, Rev. d'oto-neuro-opht. **9**:477 (July) 1931.

The author has collected the writings of the pioneer in this field, and presents a synopsis of them in an effort to make the work of this careful investigator and accurate observer more generally known. Högyes was the first to suggest the idea of a continuous action of the labyrinths on the ocular musculature, to demonstrate the disappearance of associated eye movements after bilateral destruction of the labyrinths and to suggest the value of caloric stimulation in testing the labyrinth. His experiments on animals and man in the production of nystagmus, his careful measurements and graphic records of eye movements, his amazingly accurate deductions therefrom, his study of and experiments on the intracranial pathways and his conclusions from them make a fascinating chapter in vestibular physiology. Interest in him and his work is intensified when it is realized that this work was done fifty years ago. Only the fact that his reports were buried in a comparatively inaccessible language accounts for the lack of appreciation of their value over such a long period.

After a large number of observations on reflex eye movements from labyrinth stimulation, Högyes made numerous experiments to determine: (1) those parts of the nervous system destruction of which does not cause disappearance of involuntary, associated eye movements; (2) those parts of the nervous system destruction of which does cause complete disappearance of involuntary, associated eye movements, and (3) those parts of the nervous system destruction of which causes disappearance or modification of involuntary, associated eye movements.

Then a series of stimulation experiments was made to determine those parts of the nervous system irritation of which produces bilateral associated eye movements. Mechanical, chemical and electrical stimuli were used.

He found that, "Bilateral ocular movements, deviations and nystagmus were produced by stimulation of the membranous labyrinth, the acoustic nerve, certain parts of the floor of the fourth ventricle, of the sylvian canal, of the quadrigeminate bodies and, perhaps, of the central ganglia and of the cerebral hemispheres also. If the irritation is followed by paralysis, the deviation is then to the opposite side and the nystagmus oscillations in the reverse direction."

Perhaps no more concise statement of his general conclusions from the experiments can be offered than the following quotation: "The optic nerves, the cerebral hemispheres, the central gray nuclei, the thalami, the anterior part of the anterior quadrigeminate bodies, the spinal column and the bulb below the nuclei of the acoustic, probably also the cerebellum, are not indispensable for the production of ocular movements of compensation. The motor oculi nerves, certain parts of the base of the third and fourth ventricles from the middle of the anterior quadrigeminate bodies to the acoustic nuclei, the two acoustic nerves and the membranous labyrinths are necessary for the production of bilateral ocular movements, of compensation, so called.

"In this mechanism (association of ocular movements) there are found three anatomic factors characteristic of reflex movements: the centripetal pathway of the acoustic nerve and the labyrinth, the centers in the floor of the fourth ventricle and around the canal of Sylvius and the centrifugal pathway of the oculomotor nerves. The experiments show that involuntary associated movements of the eyes are reflexes of labyrinthine origin. The center for these reflexes is in the floor of the fourth ventricle. The abolition of the ocular movements by section of the

acoustic nerves proves that they are reflex movements and not automatic. The bilaterality of the movements in unilateral lesions, the abolition of the movements by a longitudinal incision in the superior part of the median raphé prove that these pathways are, at least in part, crossed. The reflex excitations of the ocular muscles producing the movement upward and outward come from the labyrinth of the same side; those of the muscles producing movements downward and inward come from the labyrinth of the opposite side.

"The experiments of destruction make us admit that the normal state of repose of the eyes is conditioned by a continuous current of reflex excitations, going from the two labyrinths to the ocular musculature and producing a state of unstable equilibrium. This equilibrium is broken by the destruction of one labyrinth. The eyes return to their initial position after the destruction of the other labyrinth. But this second position of repose is a state of stable equilibrium, for one can no more produce involuntary ocular movements; besides, one observes also no more voluntary movements.

"The position of the eyes after stimulation of the left labyrinth, for example, is the same as that which one observes after a rotation of 90 degrees, in the frontal plane, to the left. In rotation to the left an irritation of the left labyrinth is unloosed. This fact proves anew that ocular movements produced by rotation, the destructions, the irritations of certain parts of the nervous system have a common cause and that postrotatory ocular movements are phenomena of labyrinthine irritation. Are these general conclusions applicable to man? The analogy of the anatomic structure of these parts of the nervous system makes analogy of the physiologic mechanism probable."

In the third part of the article an analysis is made of the mechanism of association in ocular movements. Högyes assumes from his experiments that a distinct bundle of nerve fibers for each ocular muscle arises in the labyrinth; that external deviation is due to the action of the external rectus muscle, internal deviation to the internal rectus, upward and downward deviation to the superior and inferior recti, respectively, and rotation to the two oblique muscles. Each muscle can contract with its homonym or antagonist of the opposite side; more than three muscles never contract simultaneously; antagonists in the same eye never contract simultaneously.

Unilateral destruction of a labyrinth causes persistent deviation of the eyes. If the left labyrinth of a rabbit is destroyed, the left eye deviates downward and inward and rotates outward; the right eye deviates outward and upward and rotates inward. The muscles involved are the left inferior and internal recti and inferior oblique, plus the right superior and external recti and superior oblique. Cutting these muscles abolishes the deviations, because they are innervated reflexly from the sound labyrinth.

Complete tables of all the functional associations of the muscles and motor oculi nerves that may occur during voluntary and reflex movements of the eyes are given in the original article.

In attempting to answer the query, "Where do the impulses from the acoustic nerves go?" Högyes encountered the great difficulties inherent in physiologic experiments in this region. From a study of the available anatomic and physiologic data, especially those from Meynert and Monakow, he deduced that, "the pathways of nervous impulses of association pass from the two labyrinths to the vestibular nuclei; next, to the nuclei of the external motor oculi muscles and thence are distributed to the other oculomotor nuclei."

A schema shows that the homolateral superior rectus, superior oblique and external rectus and the heterolateral internal rectus, inferior rectus and inferior oblique muscles are innervated by each labyrinth.

There is so much of value in this article that it would pay those who are interested to read the original.

DENNIS, Colorado Springs, Colo.

DIAGNOSTIC SCALES OF THE 1 DEGREE AND 0.17 DEGREE FORM FIELD STIMULI FOR THE EIGHT PRINCIPAL MERIDIONAL QUADRANTS TAKEN SEPARATELY. C. E. FERREE, G. RAND and M. M. MONROE, Arch. Ophth. **6**:518 (Oct.) 1931.

The purpose of this study, from the Wilmer Ophthalmic Institute, was to present diagnostic scales for the limits of the form field in the eight principal meridional quadrants taken separately for stimuli subtending 1 degree and 0.17 degree at the eye. The reason for the study was based on the fact that an eye that normally has a large field may, under the influence of a pathologic condition, suffer a considerable contraction over a comparatively small sector without reduction in the area of average breadth of the field below the critical value. In part, because of this, it has been customary to base the diagnosis on both the shape and the size of the field. However, just as there is a normal range of variation in the size of the field, so also is there a normal range of variation in its shape. For shape, then, as well as for size, a scale or standard of reference is needed for the classification of cases.

The limits were determined on a Ferree-Rand perimeter, with strict observance of all precautions prescribed for the use of this instrument. Two sizes of stimulus were used, 5.8 mm. and 1 mm. At the distance of 33 cm. on the arc of the perimeter, these stimuli subtended visual angles of 1 degree and 0.17 degree. The persons examined included private patients, physicians, nurses, assistants on the hospital staff and a large number of clinical patients. No cases showing a pathologic condition, however slight, were included in the series. Ample rest periods were allowed between observations, and care was exercised that no field was taken when the observer was suffering from general fatigue or was otherwise unfit for accurate work. Two hundred eyes were examined with the 1 degree stimulus, and 150 with the 0.17 degree stimulus. The limits were determined in eight meridional quadrants (0, 45, 90, 135, 180, 225, 270 and 315 degrees).

The group in which the 1 degree stimulus was used included 75 cases of hyperopia and hyperopic astigmatism, 30 cases of myopia and myopic astigmatism, 40 cases of presbyopia, 5 cases of mixed astigmatism and 50 cases showing either no error of refraction or an error no greater than 1 diopter of hyperopia or 0.25 diopter of hyperopic astigmatism. The group in which the 0.17 degree stimulus was used included 63 cases of hyperopia and hyperopic astigmatism, 19 cases of myopia and myopic astigmatism, 34 cases of presbyopia, 2 cases of mixed astigmatism and 32 cases, called emmetropic, which showed either no error of refraction or an error no greater than 1 diopter of hyperopia or 0.25 diopter of hyperopic astigmatism.

The results of the investigation are illustrated by charts of coordinates and in the plottings of the fields of vision. Six points are brought out. 1. The oft expressed opinion as to emmetropes and hyperopes having larger fields than myopes and presbyopes applies only when one considers the size of the field in square centimeters. When the meridional quadrants are considered separately, the breadth of the fields in the latter ametropias compares favorably with hyperopes and emmetropes. Age seems to prove a better basis for grouping than does the state of refraction. 2. The scatter or range of variation is much greater in all meridional quadrants (with the exception of the 45 degree) for the 0.17 degree than for the 1 degree stimulus. The following reasons are suggested: (*a*) Smaller differences between individuals can be detected with the 0.17 degree stimulus; that is, the stimulus of the lower visibility is more sensitive for the detection of this as well as of the other factors and variants that influence the limits of sensitivity. (*b*) The results with the smaller stimulus are more strongly affected by individual differences in refractive conditions and in the space sensitivity of the retina. The results with the larger stimulus give more nearly the range of variation in the sensitivity to light difference. (*c*) The results with the smaller stimulus are affected more by individual differences in the size of the pupil; that is, the size of the pupil is an important factor in clearness of imaging, and the small 0.17 degree stimulus

requires clearer imaging for its detection than the larger stimulus. (*d*) The results with the smaller stimulus are more affected also by individual differences in power of attention and observation than the results with the larger stimulus. Consistency of result with the smaller stimulus, even for the same observer, requires a higher degree of intelligence, training and responsibility than with the larger stimulus. 3. For the 1 degree stimulus the smallest amount of scatter occurs in the 180 degree meridional quadrant and the greatest in the 45 degree meridional quadrant. Variability in facial configuration and degree of elevation of the upper lid are probably important features in the unusually large scatter in the 45 degree meridional quadrant. For the 0.17 degree stimulus, the greatest scatter occurred in the widest part of the field. This is to be expected: (*a*) from the effect of variability of the refractive condition in the more remote portions of the field on the discrimination of a small test object, and (*b*) from the greater effect the variations of sensitivity have on the location of the limits in parts of the field where the sensitivity diminishes gradually. 4. A numerical comparison of the relation between meridional quadrants is a valuable feature in the use of scales compiled for the different meridional quadrants. This is particularly true for the 0.17 degree stimulus because of the greater range of variation or scatter of results for this stimulus, i. e., fields that were normally wide might suffer considerable contraction in one or more meridional quadrants, and still the limit might remain within the normal range of the group. 5. Because of a greater range of scatter of results, the 0.17 degree stimulus is of less value than the 1 degree stimulus for the detection of abnormalities by an inspection of the results in the various meridional quadrants considered separately. It is of no value in cases in which only the nerves that reach the far periphery of the retina are affected. The superiority of it and of other stimuli of low visibility lies (as was suggested under 4) in: a comparison of the results for the different meridional quadrants of the eye under observation; a comparison of the results for that eye with those for the other eye, and in cases in which there is a partial loss of sensitivity over a comparatively large area. For in this type of case, stimuli of low visibility show a contraction when stimuli of high visibility show nothing.

Section 6 of the summary states the values selected by the authors as designating cases that should be regarded with suspicion, excluding presbyopes. They give the standards in degrees in the meridional quadrants for the 1 degree stimulus as well as for the 0.17 degree stimulus. Excluding presbyopes, the values in the meridional quadrants, 0, 45, 90, 135, 180, 225, 270 and 315, are for the 1 degree stimulus, 84, 50, 44, 44, 52, 46, 60 and 76, and for the 0.17 degree stimulus, 54, 34, 28, 30, 34, 34, 32 and 42 degrees.

SPAETH, Philadelphia.

"AVERTIN" ANESTHESIA IN NEUROLOGIC SURGERY. WALTER E. DANDY, J. A. M. A. **96**:1860 (May 30) 1931.

During the past year Dandy has almost exclusively used "avertin" anesthesia, given rectally, for all major operations on the brain and spinal cord. After a cautious beginning because of the adverse reports from Germany, where many serious results followed the pioneer efforts, it was soon learned that not only were all the liabilities of ether entirely eliminated but every advantage of local anesthesia was also obtained. In other words, there has never been an instance of postoperative pneumonia and on very few occasions has there been postoperative nausea or vomiting. During this period, in which upward of 250 major cranial operations of every type have been performed, there has been no mortality due to the anesthetic, no instance of postoperative pneumonia, and no deleterious effect either immediate or remote. Owing to the entire absence of swelling of the brain it has been possible to modify greatly the magnitude of the cranial exposure through which certain tumors of the brain are removed. This is notably true for extirpation of hypophyseal tumors; the size of the bone defect is reduced about

one-half and without sacrificing the room that is so important for exposing and removing the tumor. Not only is the hypophyseal operation easier of performance, but also the frequent injury to the rolandic area with resulting convulsions and hemiplegia following the larger cerebral exposure is always avoided. Moreover, the danger of extradural hemorrhage, so common with the more extensive operation, is eliminated. In the approach to all intracranial tumors the same benefit, in perhaps a lesser degree, obtains. It is known beforehand that an extra allowance of bone defect will not be required to compensate for an increased volume of brain due to the effects of the anesthetic. In no procedure has "avertin" been of such paramount importance as in the author's cerebellar approach for partial section of the sensory root in trigeminal tic douloureux. The anesthetic has made it a far simpler operation because the absence of swelling of the cerebellum uniformly provides adequate room. The complete removal of cerebellopontile tumors, among the most tedious, difficult and dangerous operations and requiring the most painstaking care at every step, is especially facilitated and made safer because of the smooth regular respirations and the absence of cerebellar edema. From the patient's point of view, "avertin" anesthesia is almost ideal. Within five or ten minutes after its introduction by rectum, the patient is in a sound, peaceful and seemingly natural sleep. There has not been the slightest unpleasant sensation; there has scarcely been a movement of any part of the body. Moreover, the patient awakens gradually and rarely with any nausea or vomiting. The duration of loss of memory is several hours, frequently much of the day of the operation, thus tiding over the most uncomfortable postoperative period. Nervous patients are frequently given "avertin" in the room and are back again when awakening. Owing to the long duration of the anesthetic effects, all necessary shaving of the head may be done after the administration of the anesthetic. It is thus possible for the patient to have no memories of the operating room. How far these points of finesse are advisable depends on the probable reactions of the individual patient, but they are possible without additional risk. In no instance has there been any rectal discomfort from the "avertin." "Avertin" is by no means a fool-proof anesthetic, but it is perfectly safe if used with good judgment. The dangers have been fully enumerated by a number of German surgeons who pioneered its use. But there can be no doubt that their mortality rate has been due to overdosage, which in turn has been due to the effect to induce anesthesia with "avertin" unsupported. This is neither necessary nor advisable. The susceptibility of different individuals to the effect of "avertin" varies too much to produce maximum anesthesia safely by "avertin" alone. And, once given, the "avertin" is rapidly absorbed and beyond control. To obtain the best results with safety, an average dose should be given and any remaining deficit in the anesthesia may be overcome by supplementing a local anesthetic, either by inhalation or nitrous oxide. The amount of supplementary anesthesia, if necessary, is very small and does not change the basic character of the perfect anesthesia. For these reasons it may perhaps be preferable to look on "avertin" as a basal anesthetic; but since the anesthesia retains unchanged the full character and effects of the "avertin," this is a question of academic rather than practical interest. A safe dose of "avertin" for a normal healthy individual is from 90 to 95 mg. per kilogram of body weight. Rarely is a greater dose given and never more than 100 mg. per kilogram. Smaller doses are given when the general condition of the patient is less than normal. For an ill nourished individual, a dose as low as 50 or 60 mg. per kilogram may be adequate for complete anesthetization. Hence it is clear that each patient must be estimated individually.

EDITOR'S ABSTRACT.

THE ORGANIZATION OF TREATMENT FOR INFANTILE PARALYSIS. G. MURRAY LEVICK, Brit. M. J. **2**:652 (Oct. 10) 1931.

Treatment for infantile paralysis is discussed under two headings: the acute attack and the after-effects. During the acute attack the new anterior poliomyelitis antitoxin should be administered as early as possible, preferably within the first

few hours of the attack. It should be given partly intrathecally and partly intravenously. The author thinks, however, that it is worth while to administer this antitoxin at any time during the persistence of the pyrexia. The second important aspect of the treatment of the acute stage is to insure correct posturing of the affected parts at the outset. This is best accomplished by a method of slinging, which should be instituted as soon as the muscle pain has ceased. There is no need to wait until tenderness to pressure has disappeared.

In the pathology of infantile paralysis it is found that though there is complete obliteration of anterior horn cells, many of them are put out of action by a disturbance that falls short of complete destruction. After a time, many of the cells may recover, but their axons may have perished. A year or more may elapse during which regeneration of the axons is taking place. Thus, if the muscles are ill treated or, in many cases, if they receive no treatment at all, they may lose their contractility so that little or no muscular response can be elicited when the regenerated axons reach their destination. Therefore, a major measure in the treatment for the after-stage should be an attempt to preserve the contractility of all of the affected muscles for at least a year before hope of recovery is abandoned. The author then relates what is, in his opinion, the method of choice by which this can be accomplished. The affected muscles should be placed in the correct posture, protecting them from pressure. Properly administered electrical treatment may be of great assistance, while if improperly administered it may produce much harm. In this connection the author emphasizes that one of the greatest yet commonest mistakes in giving electrical treatment is excessive faradic stimulation. This should never be administered in the early stages of nerve recovery, when the faradic response is just returning. Only the single stimulus of an interrupted galvanic current should be used at this time. Massage, an important part of the treatment, is less likely to cause damage but, here again, harm may be done by deep effleurage. The author also emphasizes that, following this disease, the patient is frequently left in a state of profound general neurasthenia, demanding prolonged rest and constitutional treatment, including open-air nursing and heliotherapy. Local irradiation of the paretic muscles with intense red light is used as a routine measure.

Postural treatment is especially important in cases in which the muscles of the trunk are involved. In such cases, recumbency should sometimes be maintained for several years in the case of growing children. This is the only way to prevent serious spinal deformity if the abdominal or erector spinae muscles are affected to any practical extent. The author believes that the need for operative treatment, in most cases, is brought about by a lack of, or improper, physical treatment.

FERGUSON, Niagara Falls, N. Y.

THE INFLUENCE OF PAIN ON HUMAN ARTERIAL PRESSURE. RÉNÉ NYSSEN, J. de neurol. et de psychiat. **31**:205 (April) 1931.

The author has done considerable work on laboratory animals to determine the influence of pain on arterial pressure. Some of the experiments on laboratory animals were done under general anesthesia and some on decerebrate preparations. Pain caused by heat and bipolar faradic stimulation were types of the stimuli used. In man, Nyssen has determined by a series of experiments the results of actual physical pain caused by bipolar faradic stimulation, forcible pressure on the end of the finger and also the result of pain suggested to the individual in hypnosis or by autosuggestion.

It appears that pain is capable of causing a rise of arterial pressure of from 10 to 20 mm. if the pain is of sufficient intensity, though occasionally it was noted that a severe pain might cause a diminution of arterial pressure. Older persons showed a tendency to have a greater increase in pressure. This was also true of arteriosclerotic persons. There was very little difference in the pressure reaction of the two sexes. The author considers the pressure reaction general and only partially psychogenic; therefore, he thinks that emotion has little effect, and his

experiences seem to bear out his theory. Persons under general anesthesia and decerebrate laboratory animals show different pressure reactions to painful stimuli. The reaction to pain follows a short latent period of one or more seconds, the average being about six seconds. The increased tension is maintained during the whole period of pain, and appears slightly higher during the second half of the pain excitation. Following the cessation of the stimulus, the increased tension disappears gradually and at a variable rate.

Disagreeable sensations were definitely accompanied by more marked sympatheticotonic rise than subminimal painful stimuli or pleasant sensations. The arterial rise in pressure appears greater as the pain becomes greater. In this case two factors must be considered, the direct reaction to pain stimulus and the physical reaction involved. Pain stimulation in the area of hypesthesia causes less reaction than the same stimulation in normal areas. In general, painful stimulation in analgesic areas did not cause changes in blood pressure, whether the lesion was of the peripheral nerve or of the spinal cord; however, there may be a rise of pressure if the loss of sensation is cortical or thalamic. The hypothalamus may be important in the regulation of the vasomotor reaction, particularly as the result of pain, although the psychic reaction is believed to be partially responsible for the rise in pressure. It was found that in hypnosis pain as the result of suggestion gave variable results, although in general there was some hypertension. Hypertension was also present in autosuggestion, but this was not nearly as marked as was the case with real pain. Fear of pain also caused a rise of pressure, which, however, was not as marked as that caused by actual physical pain.

WAGGONER, Ann Arbor, Mich.

PHYSOSTIGMINE SALICYLATE IN THE TREATMENT OF EXOPHTHALMIC GOITER. ISRAEL BRAM, Arch. Int. Med. **48**:126 (July) 1931.

On the inadequately proved theory that the physician's most important problem in the management of hyperthyroidism is the reduction of the heart rate, Bram sought for a satisfactory cardiac sedative. Digitalis, sparteine and strophanthus were found to be of only limited service, being of value under special conditions such as complicating fibrillation, or delayed cardiac recovery accompanying general clinical improvement. His search was directed toward a preparation that would stimulate the vagus or depress the cardiac sympathetic fibers. After testing it on 200 patients, Bram concluded that physostigmine was a suitable vagus stimulant; 146 of his 200 cases presented a decided reduction in cardiac activity under the influence of this drug. These patients, however, were all subjected to rest and a high caloric diet. A group of 100 patients with hyperthyroidism received the same general treatment, but were denied physostigmine; these showed slower improvement with a greater tendency toward cyclic crises. Bram emphasizes the improvement in the exophthalmos after the administration of this drug, but he does not say how much this improvement amounted to, or in how many patients it occurred; this is an unfortunate omission, for, as the author rightly points out, the bulging eyeball is one of the most stubborn features of goiter, and any recession of the exophthalmos is indeed gratifying. Physostigmine salicylate is given in doses varying with the weight, but averaging $\frac{1}{30}$ grain (0.00216 Gm.) three times a day. The drug is administered for ten weeks. In less than 3 per cent of his cases, it was necessary to discontinue the preparation because of diarrhea.

In Bram's series the average age of the patients was 31; the basal metabolic rate was plus 46; the heart rate, 106. Patients in whom the hyperthyroidism was complicated by auricular fibrillation received 5 grains (0.324 Gm.) of quinidine sulphate three times a day, in addition to the physostigmine.

Young adults whose basal rate exceeded plus 40 received least benefit from the treatment. Greatest good was derived by those who had had the disease for many years (four or more) and those who had extreme exophthalmos. Bram also states that patients at the extremes of age (those under 14 and above 50) received more benefit than those in the medium age groups; but no figures are

quoted as to the age distribution of his patients, and the average of 31 years suggests that most of the cases were in the less benefited middle group. Except for the vague statement that "improvement occurred in the basal metabolic rate and in all subjective and objective manifestations of the disease," no figure is cited showing the percentage of improvement in metabolic rate. In Bram's opinion physostigmine is a valuable adjunct to the therapeutic armamentarium in the treatment for exophthalmic goiter.

DAVIDSON, Newark, N. J.

THE RETINA AS A NERVOUS CENTER. RAGNAR GRANIT, Arch. Ophth. **6**:104 (July) 1931.

This article is a physiologic discussion from the Eldrige Reeves Johnson Foundation for Medical Physics, University of Pennsylvania; it is in the nature of an ophthalmologic review. In the review the author outlines his conception of the retina as a nervous center and reports recent researches that show how this point of view may be used to advantage in a study of visual phenomena.

He first calls attention to Sherrington's work relative to the interaction between neurons and their synaptic interaction to reflex phenomena. Continuing with this introduction, he follows with a discussion of the work of Adrian and Matthews in reference to a study of retinal stimuli and responses. In this, the results seem to show that the frequency of nerve impulses, as obtained in the optic nerve of the conger eel, increased with the intensity of the light stimulus, and that the latent period of the outburst of impulses decreased with the strength of the light stimulus. These investigators continued their study not only of an increase of light stimulus, but also of a simultaneous stimulus of more than one portion of the retina, that is, the effect of four separated areas of illumination stimulated at the same time. A large number of well controlled experiments show that the four spots stimulated simultaneously give a higher fusion frequency than the areas stimulated singly. Here, then, is an interaction producing a retinal effect equivalent to that resulting from an increase in the intensity of illumination.

Continuing along these same lines of investigation, Granit himself considered fusion frequency and summation. These studies were applied to the periphery of the retina as well as to the area of the fovea. He found the two regions, the periphery and the center, extremely different in regard to adaptability and to sensitivity. The author further continues with a consideration of subliminal stimuli from the standpoint of summation. As he states, it is well established that a number of successive stimuli individually incapable of eliciting a scratch reflex will, by summation, develop one if repeated for some time. This was applied to subliminal stimuli of the retina.

Granit, working with W. A. Davis, in an article to the published in the *American Journal of Physiology*, will discuss this in detail. In general, the review attempts to present to the ophthalmologist a more detailed understanding of the nature and retinal localization of the physiologic processes underlying the general symptom of decreased visibility. Through this, it may be hoped that the ophthalmologist in return will be able to contribute to the difficult problems of nerve function.

SPAETH, Philadelphia.

A DEVELOPMENTAL DEFECT AND A MIXED TUMOR OF THE CENTRAL NERVOUS SYSTEM. BEATRICE CHASAN, Schweiz. Arch. f. Neurol. u. Psychiat. **27**: 64, 1931.

Chasan presents the results of a careful anatomic study of the brain of a monstrosity that lived two days after birth. The head was deformed; the left eye and left nostril were absent, the left cheek and region of the left side of the forehead being covered by a subcutaneous, tumor-like mass. The penis was of a rudimentary type. Aside from a definite microgyria, the right side of the cerebrum appeared to be normal. The left side of the cerebrum consisted of a collection of nodular masses, some of which were lobulated. It was attached at its

base to the right hemisphere, but the corpus callosum was lacking. The surface of one of the nodules on the upper and outer part of the left hemisphere resembled that of a normal cerebellum. The left cerebellar hemisphere was smaller than the right; the left pyramid was altogether lacking.

Microscopic examination of the brain stem revealed a reasonably good state of preservation of the centers essential to life. A hyperplasia of the left dentate nucleus and brachium conjunctivum appeared to compensate for the relative hypoplasia of the left neocerebellar structures. The left abducens nerve was lacking; the left third nerve was poorly myelinated and seemed to disappear in a mass of undifferentiated tissue occupying the middle fossa of the skull.

The roof of the dilated third ventricle was open and the left lateral ventricle was apparently replaced by a series of intercommunicating cystlike spaces containing a rudimentary choroid plexus. One of these spaces was surrounded by a mass of tissue containing bone, cartilage and bits of choroid plexus, as well as undifferentiated tissue. A heterotopic midbrain anlage, containing a central canal and a structure resembling the red nucleus, was also found in the substance of the left hemisphere. The cerebellar anlage on the surface of this hemisphere was of typical cerebellar structure, including a rudimentary dentate nucleus. The surface tissue anterior to the cerebellar anlage had the structure of embryonic cortex. There was an arrhinencephaly on the left, and the central portion of the visual system was poorly developed on that side.

The author believes that the developmental defects arose from "a primary, endogenous injury of the germ plasm anlage" (Keimanlage) rather than from intra-uterine disease, this belief being supported by the fact that, although the father was alcoholic, the mother had previously given birth to a monstrosity. The mass of tissue in the substance of the left hemisphere was classified as a mixed tumor rather than as a teratoma.

DANIELS, Rochester, Minn.

THE CLÉRAMBAULT-KANDINSKY SYMPTOM COMPLEX. A. A. PERELMAN, J. nevropat. i psikhiat. **1**:44, 1931.

Baillarger, in discussing hallucinations, noted that some of them lack a true sensory component, and called such hallucinations incomplete or psychic hallucinations. Kandinsky, in Russia, called them pseudo-hallucinations. In 1920, de Clérambault studied such hallucinations intensively, and came to the conclusion that they were evidences of what he called "automatisme mental." Later he described them under the symbol "syndrome S." He and his pupils established a theory that all such hallucinations were evidences of a pathologic automatism. There is a triad of manifestations consisting of sensory, higher psychic, and motor symptoms. The automatism expresses itself in the fact that the patient does not accept the various sensory experiences as arising within himself, but ascribes them to influence from without. The patient feels that the ideas which he has were suggested by somebody else, and strange thoughts were inserted by an outside power. The patient states that the psychic life is not his, and that it is controlled by an outside power. Clérambault and his school maintain that this syndrome may be associated with any clinical picture. It may be found in functional conditions, as well as in toxemias, infections and traumas. The author reports two fairly typical histories of schizophrenic patients who felt that somebody was putting various thoughts in their heads and controlled their behavior; yet they felt that the voices that they heard were not real voices but thoughts.

The author points out that the perception of "I" or the Ego is affected in these cases. The patients complain very often that the voices they hear are obsessive thoughts, and beg to be relieved of them. There is usually no insight. Claude explains this phenomenon on the basis of the fact that the patient gives a delusional interpretation to the thoughts arising within him, thus complicating the clinical picture. The author stresses the fact that one must differentiate between the primary pathogenic symptoms and secondary pathoplastic symptoms uniting with the primary. The pathogenic symptoms are due to the formal organic

involvement of the personality, as a result of which the patient dissociates his own sensations and feelings. The pathoplastic symptoms supply the specific content of the delusions and hallucinations. Personality is largely a synthesis of a large number of factors, and involvement of any one of these may give rise to a dissociation affecting the whole individual.

KASANIN, Boston.

VASCULAR SPASMS: A CLINICAL AND EXPERIMENTAL STUDY. RISER, P. MÉRIEL and PLANQUES, Encéphale **26**:501 (July-Aug.) 1931.

This long article presents several clinical cases, followed by some experimental researches on the question of the appearance of vascular spasms in the brain. The authors' conclusions are briefly as follows:

The clinical studies demonstrate the relative frequency of transitory deficit syndromes in the region of the brain or medulla, characterized by sudden appearance and disappearance, by duration from a few minutes to several hours, and usually preceding a definite lack such as hemiplegia or cortical hemianopia. For explaining these facts the hypothesis of a fleeting ischemia is the most satisfactory. These vascular spasms may attack the great trunk of the sylvian artery, before the formation of collaterals or one of the collaterals. This hypothesis of arterial spasm is rendered more probable by certain anatomicoclinical observations. Thus, the nutrient arteries that have been attacked by arteritis can become and remain permeable. The nerve tissue supplied by these vessels may develop a certain tolerance toward the relative ischemia.

This necessitates that the cerebral vessels be not looked on as passive tubes, though evidently their innervation is not especially abundant. There are undoubted cellular aggregations — microscopic autonomous ganglia which, operating on the muscular fibers within the walls, can produce a prolonged contraction, indeed even a contracture.

Experimental proofs in animals and even in man show that abrupt transitory local spasms of cerebral arteries coursing through the subarachnoid space is possible. The usual pharmacologic agents, such as epinephrine and ephedrine, do not produce an appreciable diminution of arterial caliber, but it is well known that mechanical or electrical stimulation is sufficient to produce pronounced local spasms lasting for considerable periods of time. Direct observation and microphotographic studies testify to this. The hypothesis of Foix, in which it is supposed that the lesion of arteritis itself plays an exciting rôle in producing such temporary spasms, is considered probable by these authors.

They conclude that they would not account for all transitory paralyses by arterial spasm. Thus, among other things, sudden drops in arterial tension may be causative of such conditions.

ANDERSON, Los Angeles.

RECURRENT HYPERTHYROIDISM, NEUROCIRCULATORY ASTHENIA AND PEPTIC ULCER. GEORGE W. CRILE, J. A. M. A. **97**:1616 (Nov. 28) 1931.

Thus far Crile has performed 104 operations on the suprarenal-sympathetic system. His first unilateral suprarenalectomy among a series of forty-six was performed, Oct. 1, 1913—eighteen years ago. At that time he held that in diseases due to excessive energy transformation the drive of the so-called kinetic system could be diminished by partial thyroidectomy, by unilateral suprarenalectomy and by excision of the sympathetic ganglions. He soon realized, however, that the value of thyroidectomy was limited strictly to cases of hyperthyroidism, that both lobes had to be resected or recurrence would ensue, and that in this disease occasional recurrences were seen. The same principle of compensatory function was soon noted in unilateral suprarenalectomy. Better results were obtained by a general dekineticizing operation; namely, the removal of one suprarenal, resection of the thyroid, and the excision of the cervical ganglions at the time of the thyroidectomy. Following these patients over a period of years and projecting new lines of investigation, he found that a more commanding operation was a

bilateral denervation of the suprarenal glands, the second denervation being performed a week or more after the first one. This operation will relieve and probably cure recurrent hyperthyroidism; it will relieve and probably cure with equal promptness neurocirculatory asthenia, which is a unit of pathologic physiology analogous to exophthalmic goiter. In the diseases in which emotional states, nervous strain, worry and overwork are dominating factors, such as peptic ulcer and diabetes, the principle of the operation may apply; and while the results thus far are encouraging they are not yet worked out as completely as are those for recurrent hyperthyroidism and neurocirculatory asthenia. Time and critical examination of clinical results will bring the final verdict. The author's endeavor, at this early stage, is to present the conception of an energy system which involves a group of organs that collaborate in the transformation of potential into kinetic energy. The excessive driving of this energy-controlling group or kinetic system he designates as pathologic physiology, and the surgical interventions leading to a lessening of the pathologic drive he calls a dekineticizing operation.

EDITOR'S ABSTRACT.

CHLOROFORM CONTENT OF THE BRAIN FOLLOWING ANESTHESIA. ALEXANDER O. GETTLER and HYMAN BLUME, Arch. Path. **11**:841 (June) 1931.

The problem of determining the chloroform content of the brain following anesthesia suggested itself to the authors as a direct result of a medicolegal case. The physician in whose office the patient was found maintained that he had not administered chloroform; that he performed no operation of any kind, and that the woman came to him to be treated and died before he could attend her. In order to prove or disprove these contentions, the determination of the chloroform content of the brain and lungs was of vital importance. Chloroform was present in the organs of the woman. Where was it administered? In the physician's office or somewhere else? If administered at some other place, how soon after coming out of the anesthesia did the woman feel well enough to walk? The cells continually ridding the organism of chloroform, how much chloroform could remain in the brain on her arrival at the physician's office? These are the questions that Gettler and Blume were asked to answer.

They found that, in the case of persons anesthetized for minor operations, the chloroform content is between 120 and 182 mg. in 1,000 Gm. of brain. In the case in question there was 156 mg., indicating that the deceased person was under the influence of chloroform and therefore not able to walk; hence, the chloroform must have been administered on the premises.

To prove this point, animal experimentation was resorted to. The brain of a dog killed by the excessive administration of chloroform contained 551.5 mg. of chloroform in 1,000 Gm. of tissue. The brains of animals fully anesthetized with chloroform contained 270 mg. and 284.6 mg. in 1,000 Gm. of tissue. When an animal was in the stage of recovery, the chloroform content of the brain dropped very rapidly during the first thirty-four minutes, so that only 51.3 mg. in 1,000 Gm. of brain tissue was left. From then on, the chloroform content decreased more slowly, and after one hundred and ninety minutes there was only 0.16 mg. of chloroform in 1,000 Gm. of brain. From fifteen to thirty minutes after the animals seemed normal, the brain contained from 35 to 30 mg. of chloroform in 1,000 Gm. In the stage of recovery the lungs contained much less chloroform than the brain.

WINKELMAN, Philadelphia.

NEUROGENIC FACTOR IN CHRONIC PEPTIC ULCER. WITTEN B. RUSS, J. A. M. A. **97**:1618 (Nov. 28) 1931.

The author emphasizes that the ulcer-bearing person belongs to a distinct type and from birth is predisposed to the development of chronic peptic ulcer. This type is the high-strung, emotional, so-called vagotonic person, with a sensitive nervous system and certain physical peculiarities which clearly distinguish

him from the opposite, or sympatheticotonic, type, showing marked visceroptosis, and subject to melancholia, lassitude, headaches and atonic constipation—an easy victim of morbific influences in general. Typical peptic ulcer is apt to begin in youth, or even in childhood, at the time of life when the commonly accepted causes of the disease are not present. The young ulcer-bearing person is rarely the type one expects an invalid to be. He recovers readily from acute diseases and from injuries, and is apt to be active, alert and enthusiastic in both work and play. In spite of this, he has a nonhealing, peptic ulcer. The diagnosis of ulcer in youth is becoming increasingly more frequent. The symptoms of hypermotility, hypersecretion and spasticity of the pyloric sphincter are chiefly dependent on the state of the patient's nervous system and mind, and the successful treatment of patients with these symptoms by diet, rest and alkalis merely confirms the opinion that these ulcer symptoms are dependent on the state of the patient's nervous system and occur in the vagotonic rather than in the sympatheticotonic type. It is a well known fact that patients resistant to treatment by rest, diet and alkalis often recover completely and suddenly from their symptoms when they are made happy by some occurrence. A trip to Europe, a hunting or fishing trip, or some fortunate occurrence will often cure these patients of all ulcer symptoms as if by magic. A change of residence and occupation, provided the patient is happy and contented, will result in practically 100 per cent symptomatic cures in uncomplicated cases. Ulcer patients are made worse by influences operating through the nervous system, and all other possible causes are secondary to this. They are cured, if ever, by treatment that is successful in relieving them from emotional strain and that makes them happy and contented.

EDITOR'S ABSTRACT.

THE DEHYDRATION METHOD IN EPILEPSY. D. E. CAMERON, Am. J. Psychiat. **11**:123 (July) 1931.

After studying the effect of dehydration on twelve deteriorated and noncooperative patients with advanced cases of epilepsy, Cameron concludes that the method is of little or no value in reducing the convulsions or improving the disposition of the patient. Four of his twelve subjects gave evidence of organic neurologic disorder; two had facial asymmetry and two, unequal pupils. Nine of his series had been having attacks for fourteen years or more. The average daily fluid intake under dehydration as practised by Cameron was very variable; one patient received 1,300 cc. of fluid daily for the first week. During the second week, five of the seven on whom records were available were taking over 1 liter of fluid a day. Nine patients were followed through to the end of the seventh week. Of these, five had fewer fits than at the beginning of the study, the daily averages falling in each case as follows: in one patient, the number of attacks was reduced from 4 to 1; in another, from 18 to 16; in another, from 45 to 34; in another, from 9 to 7, and in another from 23 to 3. Two showed an increase in the average number of spells (an increase of from 4 to 6, and from 3 to 11) and two showed no change. (The analysis given has been made by the abstracter from the author's tables.) In drawing conclusions from his charts Cameron says that "in some cases the number of fits is increased—in none is there a marked and constant reduction." The procedure was then reversed and fluid was forced. This failed to increase the number of convulsions; but the fluid intake under this regimen was not much in excess of the amount used with dehydration. Cameron admits that many of his patients stole water; some would drink snow; some would steal from other trays; some would drink from the flower vases. In spite of this, and in spite of the small number of patients, in spite of the reduction in the number of fits observed, and disregarding the facts that his patients were deteriorated, advanced and admittedly noncooperative, Cameron concludes, nevertheless, that the dehydration treatment is of little value in epilepsy.

DAVIDSON, Newark, N. J.

A Case of Cerebellar Abscess. Courtenay Yorke, Brit. M. J. **1**:891 (May 23) 1931.

A rather unusual case of cerebellar abscess, with a satisfactory convalescence and recovery is reported. The illness began with an ear infection, followed in two weeks by symptoms of acute mastoid disease. A few days later, acute osteitis of the mastoid was confirmed by operation, and a considerable amount of pus was evacuated. For five days the patient progressed normally. Then, vomiting and lethargy developed, but the temperature and pulse were normal and there was no headache. This was soon followed by refusal to accept food, deepening coma, incontinence, staring eyes, unequal pupils, the right being irregular, and slight deviation of the right eye downward and outward. There was no nystagmus or papilledema. The temperature was 97.5 F. and the pulse rate 76. An abscess of the brain was diagnosed, but its location was in doubt. The temporosphenoidal lobe was explored, but no pus was found. An attempt was made to explore the cerebellum, but the patient's condition became so alarming that the operation had to be terminated. The coma deepened, and lumbar puncture revealed clear fluid under pressure. After the administration of a small hypodermic of morphine (no general anesthetic), the cerebellum was again explored. Insertion of a knife in various directions to the depth of 1 inch (2.5 cm.) revealed no pus. A needle was then substituted and, at a depth of 1½ inches (3.7 cm.) a drachm of pus was evacuated. A small rubber drainage tube was inserted. Immediately, the patient improved. Fifteen days later, there was a sudden relapse, and the patient was almost moribund. The drainage tube was again inserted. Convalescence was slow but gradual. Three months later, recovery was complete.

The author's conclusions are: 1. Abscess of the brain may develop insidiously and the first intimation may be insidious coma. 2. With a hypodermic syringe, pus may be discovered when other means have failed. 3. Drainage should be continued as long as possible.

Ferguson, Niagara Falls, N. Y.

Color Changes in Fundulus, with Special Consideration of the Xanthophores. E. F. B. Fries, J. Exper. Zool. **60**:389 (Nov. 5) 1931.

In the "adaptive" changes of color of the killifish, Fundulus heteroclitus, the caudal xanthophores "expand" widely over a yellow and less widely over a black background, and "contract" over white and even more over blue. These reactions are independent of the responses to shade shown by the melanophores, which contract over yellow and white and expand over blue and black. The xanthophores are slower in response than the melanophores. The eyes are the receptors in these responses. Denervation of portions of the tail, without interruption of the circulation, results in expansion of the xanthophores in the denervated area in spite of a white background. This expansion tends to persist regardless of the color of the background, yet responses to changes in the background may occur, much more slowly than those in nearby innervated areas. Likewise, the melanophores after denervation respond to changes in the shade of the background at a slower rate and often to a lesser degree than innervated melanophores.

Interruption of the blood supply has a direct contracting effect on innervated or denervated xanthophores, probably owing to oxygen deficiency. The anesthetics ether and chloretone, applied to the gills, bring about xanthophore expansion by narcotizing the pigment-motor nerve fibers. In a denervated sector of the tail the xanthophores contract with a rise of temperature and expand with a fall of temperature.

It is concluded that the innervation of the xanthophores and of the melanophores comprises separate sets of neurons and does not form a permanently reciprocal mechanism. A discriminatory center in the brain normally regulates the responses of the chromatophores to colored backgrounds through sympathetic nervous connections. A humoral, if not strictly endocrine, controlling mechanism in certain circumstances supersedes and may normally reinforce this nervous regulation of both xanthophores and melanophores.

Wyman, Boston.

GRADING OF PATIENTS IN MENTAL HOSPITALS AS A THERAPEUTIC MEASURE. M. H. ERICKSON and R. G. HOSKINS, Am. J. Psychiat. **11**:103 (July) 1931.

For the past six months, Erickson and Hoskins have been grading the patients at the Worcester State Hospital according to behavior. Six grades are used, and the requirements for each rank are printed on conspicuous posters. Mute, resistant, excited, uncooperative patients are scored in grade "F"; lazy, careless, inadequately cooperative patients who work and play sullenly are graded as "E"; those who keep tidy, who work and play well, who are cooperative, and who seem to be getting a grasp on the significance of their old ideas are placed in grade "D." In grade "C" are listed patients on parole. These are able to acquire and understand new ideas; they are the patients who have learned to make the best of everything and to cooperate not only well, but cheerfully. Those who are reliable on parole, who work well, and who control or understand their previously distorted ideas, are classified in grade "B." From this rank, patients are sent home, where if they are able to act and work like normal people and make some adjustment to society, friends and family, they are placed in grade "A." The theme "patients are sent home only from grade B" is repeated frequently and printed on every poster.

Erickson and Hoskins report that the patients have shown much interest in this system. It uses the coloration of school room technic, and the principle of advancement and demotion according to behavior is easily comprehended. Not only do the patients themselves try to gain promotion, but their relatives take part in the process, by urging their friends to advance, by offering little rewards for promotions, and by transmitting to the patient the feeling of hope that comes with progress. The names and grading of each patient are posted and this list is studied zealously by the ward population. Feeling of group consciousness is thus promoted, and a healthy competitive spirit introduced. The plan provides additional motivation for self improvement.

DAVIDSON, Newark, N. J.

MALARIAL THERAPY OF NEUROSYPHILIS OTHER THAN UNCOMPLICATED DEMENTIA PARALYTICA. U. J. WILE and K. M. DAVENPORT, J. A. M. A. **97**:1579 (Nov. 28) 1931.

Wile and Davenport used malarial therapy in the treatment of tabes, of dementia paralytica with tabes, and of diffuse neurosyphilis, including cases complicating the secondary stage. In a large percentage of cases, immediate improvement was noted. Thus, 53 per cent of the tabetic group showed immediate improvement, and later observation increased this group to 67 per cent. In the greater number of these, improvement amounted to complete symptomatic remission. One patient showing immediate improvement relapsed later. In patients with dementia paralytica with tabes, 40 per cent showed immediate symptomatic improvement; later observation increased this figure to 67 per cent. Thirteen per cent of the cases were arrested; 13 per cent of the patients were made worse, and 7 per cent died after leaving the hospital. The immediate results were most striking in the diffuse cases affecting the central nervous system. In the group of cases complicating secondary syphilis, all eight patients were immediately improved; seven later remained asymptomatic, and in one a relapse occurred. In this case, recommended therapy was not carried out. Striking immediate improvement showed in all but one of twenty-four cases of later occurring diffuse neurosyphilis. The later follow-up of this group showed improvement in 84 per cent, no change in 10 per cent, and a change for the worse in 6 per cent. Ultimate gain in weight was an almost uniform feature, even in patients who did not otherwise improve. Following treatment, many colloidal gold curves became negative or reversed, or became more or less intense without paralleling clinical results. Reversal of the serologic reaction or diminution of its positivity occurred more often in the spinal fluid than in the blood in the group studied. Decrease in cell counts and organic solids was almost

invariably noted. From the foregoing observations it is apparent that malarial treatment is a definitely beneficial addition to the armamentarium of neurosyphilitic therapy.

EDITOR'S ABSTRACT.

PATHOLOGIC ANATOMY OF THE PALLIDAL FORM OF ATHETOSIS. M. M. AMMOSOW, J. f. Psychol. u. Neurol. **41**:374, 1931.

A boy, aged 6, who was born prematurely in the seventh month of pregnancy, began to show, at the age of 2 months, a progressive muscular rigidity associated with choreo-athetosis. The abnormal movements were predominantly athetosic. There was no history of infection, trauma to the head, difficult labor or asphyxia. A hereditary factor was suspected, but could not be definitely ascertained. The disease was undoubtedly extrapyramidal, with some features of Wilson's disease, such as dysarthria and partial dysphagia.

Histologic examination revealed definite evidences of a system disease in which the nerve fibers primarily and the nerve cells to a lesser extent presented a retrograde degeneration. The pallidum showed deposits that were well brought out by intensive staining with hematoxylin; these also gave indefinite reactions for iron and calcium. The myelin sheaths showed a peculiar scaly formation, which is regarded by Ammosow as the end-product of myelin disintegration.

The disease is considered by Ammosow as due to a congenital "weakness" of the extrapyramidal nerve fiber system. In this respect it differs from the striatal form of athetosis, in which the status marmoratus is the result of a primary destruction of nerve parenchyma, which is associated with a proliferation of glial tissue and of myelin fibers. Clinically, these two forms of athetosis are distinguished from each other by the fact that the striatal form is preeminently stationary or regressive, while the pallidal form is progressive. It may be, however, that clinico-anatomically the character of the pathologic changes is not of as much significance as the localization of the process (pallidum), so that one is perhaps justified in thinking of a form of pallidal athetosis that differs genetically as well as anatomically, although it presents no differences from a topistic point of view.

KESCHNER, New York.

ARGYLL ROBERTSON PUPILS TRUE AND FALSE. W. J. ADIE, Brit. M. J. **2**:136 (July 25) 1931.

During the course of the article, the author elaborates the statement made in the beginning that the true Argyll Robertson phenomenon is an infallible sign of syphilis; yet pupils that react in accommodation but not to light, the usual definition of an Argyll Robertson pupil, are met with in many conditions unrelated to syphilis. The essential features of a true Argyll Robertson pupil are: the pupils are small, constant in size and unaltered by light or shade, contract promptly and fully on convergence, dilate again promptly when the effort to converge is relaxed, and dilate slowly and imperfectly to mydriatics. Pupils that do not react to light but react in accommodation may be found in the following conditions: syphilis of the nervous system, nonsyphilitic congenital cerebral defects, cerebral hemorrhage and thrombosis, tumor, myelitis, arteriosclerotic and senile dementia, internal hydrocephalus, meningitis, disseminated sclerosis, trauma, syringomyelia, progressive muscular atrophy, polio-encephalitis, epidemic encephalitis, Friedreich's disease, chronic alcoholism, diabetes, nicotine and carbon disulphide poisoning and various other conditions of unknown origin. The author remarks that such a pupil has about as much value in differential diagnosis as fever or a headache. The partial Argyll Robertson sign has the same value as the complete phenomenon, but only if vision is good. Many alleged exceptions are supposed to occur. Epidemic encephalitis is supposed to be one of them, yet a critical examination of the literature and a personal examination of many patients have failed to reveal any exception to the author. Similarly, in quadrigeminal tumors, the author has

found that careful examination does not reveal a true Argyll Robertson phenomenon. The author concludes that the true Argyll Robertson pupil, as he has defined it, is, as near as may be in an imperfect world, an infallible sign of syphilis of the nervous system.

FERGUSON, Niagara Falls, N. Y.

ISOLATED PARALYSIS OF THE HYPOGLOSSAL NERVE. N.-A. GOLDENBERG and J. G. SANDLER, Rev. d'oto-neuro-opht. **9**:429 (June) 1931.

The rarity of isolated paralysis of the hypoglossal nerve warrants the publication of this case. A married woman, aged 28, complained of pain in the throat on swallowing, difficulties of speech and mastication and swelling of the right half of the neck, which had begun five days previous to examination, with pain in the throat. There had been no previous illness. The temperature was subfebrile. The following observations were made: a moderately hard tender swelling, extending from the angle of the mandible to the lobe of the ear on the right side; edema and infiltration of the right tonsil and adjacent palate; deviation of the tongue to the right when protruded and of the point to the left when in place, and exaggeration of faradic excitability on the right side of the tongue. All other results of examination were negative. At the end of three months, the symptoms had disappeared.

The isolation of the paralysis points to a peripheral lesion, although a single case of isolated, bilateral paralysis of the hypoglossal nerve, caused by syphilis, has been reported. Lesions of the nerve between the medulla and its canal are usually caused by destruction of the bone, and the tenth and eleventh nerves are usually involved also. Lesions peripheral to the emergence of the hypoglossal nerve from the canal are the most frequent causes of paralysis. The etiology is varied: tabes, syringomyelia, disseminated sclerosis, poliomyelitis, diseases of the vertebrae and base of the skull, tumors, tuberculosis and trauma. Phlegmonous angina and enlargement of the cervical lymph nodes are very rarely the cause of glossoplegia. Nevertheless, the authors believe that such an etiology is possible, and that in their case these factors played an important rôle in causing the neuritis.

DENNIS, Colorado Springs, Colo.

PARALYSIS OF THE BRACHIAL PLEXUS FOLLOWING SERUM THERAPY FOR DIPHTHERIA. H. ROGER, C. MATTEI and J. PAILLAS, Ann. de méd. **29**:610 (May) 1931.

Nine cases of paralysis of the arms, including three cases personally observed, following injections of diphtheria antiserum were analyzed. All the reports were published in the French literature. Adults (from 16 to 34 years) only were affected. Following the injection of an average dose of from 20 to 60 cc. of antiserum, generalized urticaria, edema of the legs and fever and pain, arthritic in type, developed. The pain receded and was finally localized in the upper part of the shoulder. A flaccid paralysis of the shoulder and the upper part of the arm followed, with a diminished reaction of the muscles to electric stimulation and sometimes complete reaction of degeneration. Next, muscular atrophy was noticed and persisted for a long time, even after the regaining of function. Disturbances of sensation were usually added to the picture of motor paralysis; there were complaints of burning, lancinating pains or of simple paresthesias. Objectively a mild hyperthesia, with transition to anesthesia, was found with a predilection for the area of the cutaneous branch of the circumflex nerve. Motor and sensory disturbances remained stationary for many months, and complete recovery occurred very slowly.

There can be no doubt that this type of paralysis is not produced by the diphtheria toxin directly. Sicard and de Gennes considered it as an allergic phenomenon, and thought that urticaria and edema produced this lesion of the more sensitive nerves of the brachial plexus. Other authors assumed a lesion in the spinal cord. Lhermitte was in favor of a radicular origin; others considered

it a peripheral lesion. Such accidents may be prevented either by the use of purified and albumin-free antiserums, preceded by injections of carbonates or citrates. The treatment consisted of electrical stimulation in connection with strychnine.

WEIL, Chicago.

TRYPARSAMIDE THERAPY. JULIA LICHTENSTEIN, Arch. Dermat. & Syph. **24**: 182 (Aug.) 1931.

To determine the value of tryparsamide therapy, seventy-six ambulatory patients who had tabes, dementia paralytica and meningovascular syphilis were studied. In the group with dementia paralytica was a woman, aged 39, who had had the disease for ten years; she had been treated previously with mercury and arsphenamine. After she had received twenty-five injections of tryparsamide in a year and a half, the Wassermann reaction changed from 4 plus to negative, the colloidal gold curve flattened out to a line of zeros, and the patient was so much improved clinically that she could return to work. Ten male patients with dementia paralytica, all of whom had been treated with other antisyphilitic preparations before, were given an average of twenty-five injections of tryparsamide; in five of these, the Wassermann reaction decreased or became negative, and 81 per cent were much improved clinically. Fifteen patients with meningovascular syphilis received on an average twenty-seven injections of tryparsamide; eleven improved, and the other four did not. Seven women with locomotor ataxia were each given fifteen injections of tryparsamide; four patients improved and three did not. However, only the patients with advanced cases failed to show improvement. Thirty-four male tabetic patients received twenty-two injections of tryparsamide each; seventeen improved and seventeen did not.

Lichtenstein believes that the danger of ocular complications from the use of tryparsamide has been exaggerated. She suggests giving the injections in doses of 3 Gm., at weekly intervals, with eight injections in a series. In the whole group of cases, 77 per cent showed clinical improvement, a result that entitles tryparsamide to much consideration in the treatment for neurosyphilis.

DAVIDSON, Newark, N. J.

INFERIOR HEMIANOPIA FROM RETINAL EMBOLISM AND ANGIOSPASM. AUBARET, Rev. d'oto-neuro-opht. **9**:507 (July) 1931.

A woman, aged 32, suddenly became blind in the left eye on December 24. A few days later, vision began to return in the upper part of the field. After ten days, visual acuity was 1/100, the inferior part of the visual field was abolished, and the superior half was reduced in the periphery. The ophthalmoscope revealed a milky edema, limited to the upper part of the retina of the posterior pole; its lower border was horizontal and it covered the macula, which was quite red. The patient was given injections of acetyl choline, retrobulbar injections of atropine sulphate and cyanide of mercury intravenously. Visual acuity improved and became almost entirely normal by February 19; the superior part of the visual field was normal except for a notch at the point of fixation, but vision in the inferior half of the field was still abolished, and the papilla was becoming atrophic.

About this time, another patient was seen who, eight years previously, had suddenly become blind in the right eye. The blindness was of short duration, and no oculist was consulted. Examination showed complete loss of the inferior part of the right visual field, almost identical with that in the first case, normal pupillary reactions (except that there was no reaction when the light was projected onto the superior part of the retina) and a discoloration of the papilla, which was more marked in its lower half.

The diagnosis in both cases was embolus or angiospasm of the central artery of the retina or its two branches. The cause was not determined. It is interesting

that, in these cases of limited ischemia, central vision can recuperate but the visual fields show signs of permanent damage. This explains the persistence of these hemianopias and the other alterations of the visual fields.

DENNIS, Colorado Springs, Colo.

RECURRENCE OF TUMORS IN THE SPINAL CORD. I. BÜRKNER, Arch. f. Psychiat. **92**:167, 1930.

Bürkner reports three cases of spinal cord tumor in which there was a recurrence of the growth after operation. In case 1, a woman, aged 50, presented typical signs of a tumor of the cord; an operation was performed and a well circumscribed extramedullary tumor was removed, following which the symptoms disappeared. Four and one-half years later, the symptoms again developed, pointing definitely to a recurrence of the tumor. The patient, however, refused a second operation. In case 2, that of a man, aged 54, an operation was performed for an extramedullary glioma, which was apparently totally removed; eleven months after the operation, however, there was a gradual recurrence of symptoms with some indication of increased intracranial pressure. Other metastases occurred, and the patient died. In case 3, that of a girl, aged 19, an extramedullary, perivascular sarcoma at about from the eighth to the tenth dorsal vertebra was removed. Three and a quarter years after the operation, the symptoms recurred; operation was not possible and the patient died. At autopsy, a spreading of the tumor along the canal from the tenth dorsal to the seventh cervical vertebra was found.

The author reviews sixteen additional cases that have been reported in the literature and comes to the following conclusions: There is recurrence of tumors of the spinal cord in a surprisingly small percentage of cases. This would suggest that spinal cord growths are not as malignant as are tumors elsewhere. However, since recurrences are found, both in benign or malignant growths, it would be a good plan to subject the patient to roentgen treatment following the operation. This does not always prevent a recurrence, but is worth trying.

MALAMUD, Iowa City, Iowa.

HETEROPLASTIC TRANSPLANTATIONS OF EMBRYONIC SPINAL-CORD SEGMENTS IN AMBLYSTOMA. S. R. DETWILER, J. Exper. Zool. **60**:141 (Aug. 5) 1931.

The method of heteroplastic grafting of organs between animals of two different species possessing different rates of growth was used. When the brachial portion of the spinal cord of Amblystoma tigrinum embryos is substituted for the corresponding region in embryos of Amblystoma punctatum, the graft, in larvae ranging from 32 to 60 days of age, shows complete regulation so as to correspond in size and cell numbers with this portion of the normal punctatum cord. In the reciprocal experiments regulation has also been found to take place. Compared with other heteroplastic grafts, this regulation occurs much earlier. The difference in the size and cell numbers of corresponding cross sections between the normal spinal cords in larvae of the two species, which present extreme contrasts in size, is not as great as might be assumed. Evidence is at hand to show that in a punctatum larva of 21 days the tigrinum cord graft grows at a velocity that is considerably greater than the host rate. The data indicate that regulation takes place approximately within the first four weeks. When the first three spinal segments of the tigrinum cord are substituted for the punctatum brachial region, complete regulation does not occur. The graft undergoes extensive development in size and cell numbers, behaving in a manner similar to that of the corresponding region of a punctatum cord when grafted homoplastically to the same position. In the latter instance, the presence of the graft in the brachial region stimulates overgrowth and extensive production of cells in the intact first and second segments of the cord. In the case of the tigrinum graft this effect is very slight. Larvae with composite heteroplastic cords experience no greater difficulty in metamorphosing than do normal animals.

WYMAN, Boston.

A Case of Acrodynia (Infantile) of Selter-Swift-Feer in a Youth Aged 19. F. Pennacchi, Riv. di pat. nerv. **37**:126 (Jan.) 1931.

The author reports the case of a man, aged 19, who previously had been normally developed both physically and mentally, and whose behavior gradually modified so that in a few weeks he became mute, indifferent and negativistic, and had incontinence of urine and obstinate constipation. Neurologically, there were some muscular atrophy of the hands and some hypertonus. There was considerable hyperhydrosis, involving particularly the head, hands and feet. The pupils were enlarged and sluggish in reaction. Saliva was abundant. Three months later, a trophic condition of the feet, represented by desquamation developed. The skin of the feet was cyanotic. Later, desquamation was noticeable also in the palms. In his attempts to walk, the patient disclosed great carefulness and slowness, and walked as if he had pain in the feet.

The author discusses the symptomatology and pathogenesis of the condition, and concludes that the case should be classified as acrodynia as described by the French author Chardon in 1828, described later by Selter in 1903 under the name of trophodermatoneurosis, eleven years later by Swift under the name of erythroedema and in 1921 by Feer under the name of neurosis sui generis of the vegetative system. Though the reports of cases in Europe, America and Australia deal essentially with the infantile form, the author believes that his case may belong to the group of acrodynia. The author believes also that from the pathogenic standpoint the condition is due to a virus infection similar to, but not identical with, that of epidemic encephalitis, which enters the body through infection of the rhinopharynx. The infection seems to have a predilection for the vegetative centers of the diencephalon and mesencephalon.

Ferraro, New York.

The Effects of Experimentally Induced Anesthesia of the Extra-Ocular Muscles in Man. A. E. Kornmüller, J. f. Psychol. u. Neurol. **41**:354, 1931.

Retrobulbar injection of procaine hydrochloride and of epinephrine hydrochloride into the recti muscles (or into their tendons) of the right eye was followed by:

1. A clinical picture of almost complete paralysis of all the muscles of the eye receiving the injection.

2. A sensation of a deviation forward or of an advancing of the right shoulder, which was experienced only immediately after the injection.

3. On looking at objects only with the anesthetized eye while the head and body were in motion, the objects appeared to move in directions opposite to those of the head and body; this is attributed to a failure of the compensatory mechanism of the extra-ocular muscles as a result of the anesthesia.

4. Marked alterations in the egocentric optic localization during voluntary vision with the anesthetized eye.

5. On looking only with the anesthetized eye at a bar mounted on a rotating chair, the bar, as well as its optic afterimage, produced no changes in the localization of the bar; this is in contrast to what happens under normal conditions.

6. During rotation of an "optical turning wheel," the perception of "self-movement" was less marked, and the egocentrically determined movement of the rotating stripes in the wheel was more marked, than normally.

7. On looking with the almost immobile right eye at the passing stripes of a rotating wheel, there was observed a typical optic nystagmus in the covered left eye.

Keschner, New York.

The Rôle of Physical Conditions in Behavior Problems. Arthur Timme, Ment. Hyg. **15**:468 (July) 1931.

The medieval idea that crime and insanity are controllable deviations, deserving of punishment, has not yet entirely disappeared. However, with the advance of

pathology and physiology in the nineteenth century, emphasis was placed on behavior disorders associated with physical conditions, such as the irritability of hyperthyroidism, the expansiveness of the patient with dementia paralytica, and the moria of the patient with a tumor of the frontal lobe. While there is danger of oversimplifying by searching too closely for a simple physical agency, this factor must always be kept in mind. Timme gives two examples—a boy with hypopituiary obesity whose organic defect caused a craving for sweets, and whose environment made satisfaction impossible. This child stole change to buy candy and to impress his playmates. He also cites the example of a child with a strabismus who, to prevent constant teasing, became a fighter. The fact that these disorders are not simply organic or simply psychogenic, but of a rather complex origin must always be borne in mind. Among the physical defects that frequently give rise to behavior disorders, Timme mentions measles, mumps, malnutrition, chronic infections, orthopedic deformities, encephalitis and endocrine defects. He warns that these factors must not be overemphasized to the point of neglecting the social agencies and environmental problems that may be responsible for the condition. In a propery balanced point of view, the physical condition is considered the starting point acting because discrepancies in the social situation, home environment or emotional attitude fail to provide adequate compensatory satisfactions.

DAVIDSON, Newark, N. J.

AN EXPERIMENTAL STUDY OF THE INDEPENDENT DIFFERENTIATION OF THE ISOLATED HENSEN'S NODE AND ITS RELATION TO THE FORMATION OF AXIAL AND NON-AXIAL PARTS IN THE CHICK EMBRYO. T. E. HUNT, J. Exper. Zool. **59**:395 (May 5) 1931.

Chorio-allantoic grafts of isolated levels of the area pellucida of chick blastoderms in the definitive primitive streak, advanced head-process and from one to twelve somite stages were studied. The results showed that the node level of each stage forms specific parts and is the only level of the primitive streak that has any marked capacity for organ differentiation. A graft containing the node in the definitive primitive streak stage forms all levels of the brain, spinal cord, notochord, eye, epiphysis, hypophysis, heart, liver, mesonephros and the nonspecific structures, such as intestine, cartilage, muscle and integument. In later stages, the capacity of the node level is restricted, since it no longer forms anterior parts. This restriction continues until the somite stages, at which time the capacity to form trunk structures, such as spinal cord, mesonephros and suprarenal gland, increases.

Grafts of the primitive streak posterior to the node do not form organs but only nonspecific tissues. Grafts of the level anterior to the node likewise form only the nonspecific tissues. If a part of the node is transplanted with the primitive streak, organ-specific parts will form, such as the neural tube, notochord and mesonephros. It is concluded that the principal rôle of the node is the formation or induction of axial parts, i. e., neural tube and notochord. Evidence is also presented that suggests that the head-process induces the formation of the medullary plate.

WYMAN, Boston.

SEX PERVERSIONS IN ANIMALS. BASTIAN SCHMID, Fortschr. d. Med. **49**:425 (May 29) 1931.

Anomalies of sexual behavior in domestic animals are not rare phenomenon, particularly where there is unequal division of the sexes. Cows during heat have been known to mount one another when there are no steers, and monkeys in captivity frequently resort to masturbation. Eulenstein has described sexual excitement of doves pressing the claws against the human finger and going through the motions of wooing. Schiller has described actual sexual intercourse between

female cats and male rabbits that had grown up together. The substitution of another male rabbit did not, however, lead to any sexual activity. In another instance a monkey acted as midwife for a cat in labor and produced a miscarriage by attempted intercourse. Male frogs show a considerable lack of specificity in their sexual embraces and may cling to a stick of wood in reflex fashion, which hardly deserves the application of the term perversion. Female spiders have shown a cannibalistic relish for the males which after fertilization has taken place seem to be superfluous. Young goats have been observed attempting cohabitation with their mothers. The author describes an instance of a peacock that frequently attacked women and had to be beaten off. Many of these perversions, he states, disappear when opportunities for normal sexual behavior are available.

HART, Greenwich, Conn.

"FUGUE" FOLLOWING A SEVERE ELECTRIC SHOCK. DIVRY and CHRISTOPHE, J. de neurol. et de psychiat. **31**:302 (May) 1931.

In a man, aged 27, without important personal or hereditary antecedents, amnesia developed after a severe electric shock. After the disappearance of the acute phenomena there was a phase of depression characterized by suicidal ideas; he then fled from his surroundings and attempted suicide. Following the amnesic period, the patient had only imperfect memories of what had happened. The amnesia was, therefore, partial or relative. During the period immediately after the shock and before the amnesic period, the patient complained of severe pain in the head and other parts of the body, with marked tenderness over the nerve trunks. Curiously, the pain and tenderness were much more marked in the left arm, through which he had received the shock. The authors presume that the patient had a severe radicular irritation with consequent increasing pressure of the spinal fluid. Drainage of the spinal fluid relieved the symptoms. No motor phenomena of any kind were observed. From a psychiatric point of view the patient presented, in addition to the depression and flight, asthenia, palpitation, tremors, etc., similar to those observed in traumatic neuroses. The authors assume that the symptoms presented by the patient are much more like those of hysteria than those of a true psychotic state.

WAGGONER, Ann Arbor, Mich.

THE HEMATO-ENCEPHALIC BARRIER. S. KATZENELBOGEN and H. GOLDSMITH, Am. J. Psychiat. **10**:1045 (May) 1931.

To determine the permeability quotient, Katzenelbogen and Goldsmith administered bromides, 3 Gm. daily, for five days, and on the sixth examined the bromide concentration in the blood and spinal fluid. The normal permeability quotient falls between 2.9 and 3.3. In the literature cited, the permeability quotient is reported as being low in the organic psychoses, high in dementia praecox and normal in the affective psychoses. The work of Katzenelbogen and Goldsmith failed to substantiate this, however. In each group, most of the permeability quotient's were normal, although whatever discrepancies there were in the organic group were for the most part on the low side. Seventy-five per cent of the schizophrenic patients had a normal permeability quotient, and most of the remaining cases showed a high quotient. In patients with manic-depressive psychoses, 60 per cent had normal permeabilities, the remaining 40 per cent being equally divided in high and low quotients. A similar distribution was found in persons mentally defective. Age did not appear to affect permeability. From these observations the authors conclude that modifications in permeability of the hemato-encephalic barrier are not characteristic of any psychotic type.

DAVIDSON, Newark, N. J.

STUDIES OF BROMIDE DISTRIBUTION IN THE BLOOD. II. THE DISTRIBUTION OF BROMIDES AND CHLORIDES IN THE BLOOD OF DOGS FOLLOWING THE ORAL ADMINISTRATION OF SODIUM BROMIDE. H. B. VAN DYKE and A. BAIRD HASTINGS, J. Biol. Chem. **92**:27, 1931.

When sodium bromide was administered to dogs by mouth, analysis of the blood revealed a much higher bromide and a much lower chloride concentration within the red blood cells than would have been expected on the basis of the experiments in vitro. The bromide distribution ratios were nearly always higher than the chloride ratio. Bromide ratios as high as 2 were sometimes observed and ratios between 1 and 2 occurred quite commonly. The chloride ratios were commonly less than the normal value of 0.7 and often as low as 0.5. When serum of a bromide-fed dog was mixed with the cells of a normal dog, the bromide tended to distribute itself as in the experiments in vitro. When, however, the cells of a bromide-fed dog were mixed with the serum of a normal dog, the bromide distribution ratio obtained was high, similar to those occurring in experiments in vivo. This suggests a tendency on the part of cells from bromide-fed animals to retain their bromide.

FREMONT-SMITH, Boston.

THE INFLUENCE OF THE NERVOUS SYSTEM ON REGENERATION IN NEREIS VIRENS, SARS. GLADYS ELIZABETH HOLMES, J. Exper. Zool. **60**:485 (Nov. 5) 1931.

Posterior regeneration of segments in Nereis virens, Sars, is normal if the ventral nerve cord is present at the cut surface. Without the ventral nerve cord at the cut surface, in 61 per cent of the cases no regeneration occurred. In 39 per cent of the cases abnormal posterior regeneration occurred. Two cases suggest that nerve tissue other than the ventral nerve cord may possibly influence posterior regeneration. Injury to the tissues in general does not account for the absence of normal regeneration. Normal regeneration can take place even though the union of the ventral nerve cord with the cephalic ganglion is interrupted, provided the nerve cord is still intact at the cut surface. While the presence of the nerve cord is not essential for the growth of new tissue at the posterior cut surface in Nereis, it is evident that it is necessary for complete organization of the new tissue.

WYMAN, Boston.

OCULAR SYMPTOMS IN THE DIAGNOSIS OF TUMOR OF THE BRAIN. W. D. ABBOTT, Arch. Ophth. **6**:244 (Aug.) 1931.

This paper is an ophthalmologic and otolaryngologic contribution, presented for the purpose of classifying the symptomatology of lesions in the optic tract, i. e., of the optic nerves themselves and of the chiasm, the primary visual centers and the radiation of Gratiolet. The author discusses briefly ophthalmologic pictures, fields, pupillary reflexes and other generally allied symptoms. Two tables conclude the article, in which lesions of the pons, midbrain, cerebellum and medulla are classified from the standpoint of their location, the type of syndrome and the neurologic and ophthalmologic signs and symptoms. In these tables, lesions of the pineal gland, the third nerve nucleus, cerebellar tumors, red nucleus, cerebral peduncle, the pons at the level of the sixth nerve, at the level of the sixth and seventh nerves, at the level of the seventh nerve, and the cerebellopontile angle are all illustrated. In table 2, under a similar classification, symptoms are presented of lesions of the temporal lobe, the parietal lobe, the occipital lobe and the basal ganglia.

SPAETH, Philadelphia.

THE NEUROTROPISM OF THE VIRUS OF DENGUE. E. AVARITSIOTIS, Ann. de méd. **30**:5 (June) 1931.

The following facts were cited in support of the theory that the dengue virus has a specific affinity for the nervous system, and that changes in other organs of the body may be explained by the vegetative disturbances: at autopsy, failure of the viscera to show any inflammatory reactions; normal spinal fluid in the presence of a definite clinical picture of meningitis; the sudden formation of multiple abscesses, which are not inflammatory, but rather aseptic; the long persistence of certain symptoms during convalescence—bradycardia, precordial and thoracic pains, epileptiform attacks, and insomnia; the sudden onset of multiple vascular disturbances in the skin, like multiple hemorrhages following constriction of the arm with the rubber arm-bag of the sphygmomanometer, local congestion and pruritus. It should be emphasized that this conception of dengue as a neurotropic disease is based mainly on clinical observations, and that detailed autopsy reports are still lacking.

WEIL, Chicago.

SOME CLINICAL RESEARCHES IN NARCOLEPSY. S. WOHLFAHRT, Acta psychiat. et neurol. **6**:277, 1931.

The author reports four cases of true narcolepsy (i. e., cases showing the narcoleptic syndrome without any ascertainable cause), three of narcolepsy following epidemic encephalitis and one occurring in an epileptic patient. He thinks that, as in the case of epilepsy, there is not a narcolepsy but narcolepsies. From a review of the literature and from his own studies he found that the majority of cases of true narcolepsy showed a decreased metabolism, indicating some dysfunction of the vegetative nervous system, and he thinks that the cause may lie in some lesion of the anterior lobe of the hypophysis or the hypothalamic centers. The findings in the encephalitic cases also appear to indicate a lesion situated as described, as well as lesions in the gray matter of the wall of the third ventricle. He thinks that his suggestions are purely speculative, because knowledge of the mechanism of ordinary sleep is so incomplete.

PEARSON, Philadelphia.

MANIPULATIVE REDUCTION OF CRUSH FRACTURES OF THE SPINE. R. WATSON JONES, Brit. M. J. **1**:300 (Feb. 21) 1931.

A simple, practical method for the reduction of injuries of the spine and their treatment is recorded. The success of this method is dependent on hypertension of the spine, secured and maintained by placing the patient with his hips on one table and his folded arms and head on another table, slightly elevated, and then applying a cast in this position, which is to be worn for four months. After ten days, in the usual case, the patient may get up and walk for short intervals. Naturally, the ideal time for reduction is the first day, but the author reports successful results by this method even ten days after an injury. In regard to the first-aid treatment of such patients with crush fractures, the author advises that they be carried face downward, supported at the hips and shoulders, some degree of sagging being allowed between the points of support.

FERGUSON, Niagara Falls, N. Y.

THE MOTOR DEVELOPMENT OF CHILDREN SUFFERING FROM STAMMERING: THE NEUROPSYCHIATRIC PROBLEMS OF ADOLESCENCE. COLLECTED PAPERS. Ukrainian State Neuropsychiatric Institute **16**:81, 1931.

Fifty school children who stammered were studied from the point of view of intelligence and motor endowment by the methods of Ozeretzky and Quint. The children were both male and female, and varied in nationality, race and age. The following conclusions were reached. (1) The intellectual development is usually above normal; (2) the motor development is considerably ahead of the chrono-

logic age; (3) the inadequate motor development found in some cases is usually associated with mental deficiency; (4) stammerers who are well developed intellectually are also well developed from the motor point of view; (5) the mimicry and facial expression are affected by stammering.

KASANIN, Howard, R. I.

A CASE OF ACHONDROPLASIA. VICTORIO CHALLIOL, Arch. gen. di neurol. e psichiat. **11**:349, 1930.

A patient, aged 13, 112 cm. tall and weighing 30.6 Kg., presented a typical picture of achondroplasia. Photographic and x-ray plates were demonstrative of the condition. There was moderate mental deficiency. The patient also had a spina bifida occulta. Neurovegetative tests gave a distinctly vagotonic response: high basal metabolism (+32); low p_H of the urine (6.2). The Wassermann reaction of the blood was negative. The author emphasizes the signs of endocrinovegetative disturbance (hyperthyroidism with vagotonia) presented by his patient. He regards this disturbance as one possible factor in the production of the syndrome of achondroplasia.

YAKOVLEV, Palmer, Mass.

NEURORETINITIS ASSOCIATED WITH NEPHRITIS AND HYPERTENSION. J. ROLLET and PAUFIQUE, Ann. d'ocul. **167**:773 (Sept.) 1930.

Six cases of neuroretinitis associated with nephritis and hypertension are reported by Rollet and Paufique. None of the patients showed an increase in the urea or uric acid content of the blood, and the authors think that the lesions are best explained by arterial hypertension or hypertension of the cerebrospinal fluid. Among other causes they speak of the retention of chlorides in the central nervous system and the retina ("la retention chlorée"). They are inclined to agree with certain other authors that the retinitis is not secondary to the renal lesion but accompanies it.

BERENS, New York.

CLASSIFICATION OF BRAIN TUMOURS AND ITS PRACTICAL APPLICATION. WILDER PENFIELD, Brit. M. J. **1**:337 (Feb. 28) 1931.

A condensed abstract of this valuable paper is not possible. The author reports the most commonly accepted classifications of brain tumors, with special reference to the glioma group. It is of particular interest to all physicians engaged in neurologic practice and especially those of the neurosurgical group.

FERGUSON, Niagara Falls, N. Y.

THE INFLUENCE OF THE SYMPATHICUS ON THE STRIATED MUSCLE. K. SCHNEIDER, Arch. f. d. ges. Physiol. **227**:293, 1931.

The influence of a stimulation of the rami communicantes on the form of the single contractions and on the action currents of the muscle was studied. The author was unable to find such an influence.

SPIEGEL, Philadelphia.

Society Transactions

PHILADELPHIA PSYCHIATRIC SOCIETY

Regular Meeting, May 8, 1931

FREDERIC H. LEAVITT, M.D., *President, in the Chair*

WILLIAM BLAKE: "MAD" BLAKE AND HIS TREE FULL OF ANGELS. DR. ROBERT L. PITFIELD.

William Blake (1759-1828), poet and engraver, was of a singular mental make-up. A few friends and acquaintances thought him to be insane, and so he was called "mad" Blake throughout his adult life.

He became a distinguished artist and poet. His engravings are famous. A chief characteristic was that he was a deep mystic in art and later in poetry. Early in life he began to exhibit hallucinatory tendencies. At the age of 9 years he told his parents that he had seen a tree full of angels. This hallucinosis evidently continued throughout his life. He claimed that his brother revealed a new process of engraving to him. His fame grew as he progressed in poetry and engraving, but he made little money and was always poor. He was of a gentle nature and given to doing humane and kindly deeds. His later poetry was so obscured by mysticism and so ugly in form that it never has had a popular vogue. As a minor poet he has first rank in English literature. Many of his contemporaries were emphatic in saying that he was not insane. It appears that he was of that singular company who during life have received an inward illumination that alters their conduct and beliefs ever afterward.

DISCUSSION

DR. CHARLES W. BURR: I think that Blake's "madness" was the "madness" of the gods, and what we men of the twentieth century call the madness of genius. His chromosomes and qualities were different and greater than those of average men.

DR. JAMES HENDRIE LLOYD: If I were asked to describe Blake, I should say that he had schizophrenia. He had a "split mind," and only a part of it acted normally. For instance, he had great technical skill as a draughtsman and engraver. Any one who looks at Blake's engravings must acknowledge that he had a fine technic. But his skill was perverted. He used his ability to draw grotesque or horrid pictures. One of them is a picture of Eve, a naked woman, with a snake coiled around her body and holding the snake's nose up to her nose. In other words, the man knew how to use his hand, but he did not know how to use his mind. His thoughts were perverted, and he had the most extravagant and fantastic beliefs. One cannot say that he was normal, and yet he was not sufficiently insane to be shut up in an asylum. I think that the best poem Blake ever wrote was his poem on the tiger, in which he presents the problem of evil, which has forever baffled the minds of men: "Did He who made the lamb make thee?"

DR. EDWARD A. STRECKER: What appealed to me in Dr. Pitfield's presentation was not only the story but the kind way, differing somewhat from the tendency of other modern writers, in which he mentioned only the fine things of Blake's genius.

DR. ROBERT L. PITFIELD: As to Blake's insanity, I derived my opinions from his many biographies and the diaries of two men. I think that one good explanation of his mental state is that he belonged to the "illuminati," a group of kind, thoughtful, wonderful people who were abnormal in their reactions to life about them. He was not blameful or persecutory in his tendencies toward other men; therefore, he had no paranoic tendency.

THE CLINICAL APPROACH TO THE PROBLEM OF MENTAL DEFICIENCY. DR. HOWARD W. POTTER, NEW YORK.

The term "mental deficiency" should not be used in a clinical sense, as it is chiefly a medicolegal concept. Like the term "insanity," mental deficiency denotes merely a social group of persons who are mentally deficient because of the presence of a wide variety of pathologic conditions that have as one, and only one, of their symptoms a defective or deficient intelligence. Attention has been called to the inadequacy of the present purely psychologic scheme of classification of mentally defective persons and it is denied that it is in any sense a clinical classification.

In laying a basis for a clinical approach to the problem, I have shown how the intelligence, in order to be fully integrated, is dependent on the adequacy of structural, metabolic and emotional factors, and that a breakdown or failure in any one of these factors may result in an ineffectively functioning intelligence, the only symptom common to all hypophrenias. The hypophrenias may be grouped under three different headings on a pathogenic basis: constitutional, reactional and degenerative. Within each of these large groups are found various groups or clinical types. A clinical attitude should be maintained for the most part from a psychobiologic point of view.

DISCUSSION

DR. LEROY M. A. MAEDER: I have been interested in hearing Dr. Potter present these wholesome and broad points of view on feeblemindedness. It has been my belief that feeblemindedness has been considered in the light of social or psychologic diagnoses. There has been a tendency to label a child with an intelligence quotient on the basis of the progress made at school; then after he was termed an idiot, imbecile or moron, it has been thought all that was possible was done and that all that remained was to place him in an institution. The problem should be looked at from a more physiologic point of view, as it has been presented here.

DIAGNOSIS, TREATMENT AND TRAINING OF THE FEEBLEMINDED. DR. HARVEY M. WATKINS, POLK, PA.

In pointing out the many-sided problems of feeblemindedness, one must stress the medical point of view as to etiology, in addition to stressing the fact that the condition presents a psychologic, pedagogic, social and legal problem. The complete history, including the family history and particularly the personal and developmental history, should be stressed, and special attention should be given to injuries at birth and to diseases occurring before the fifth year. Mention should be made of certain important factors: the results of physical examination, particularly regarding the endocrine glands, and the history of progress in school, together with the examination of school work and of practical knowledge. Careful inquiry into the economic efficiency of those who are beyond school age and a knowledge of the type of person as regards social history and moral reactions are important. Complete psychometric tests should be made in all cases, and these tests should be repeated yearly or oftener, as needed, during residence in state schools. A complete examination should include all of the various factors, and a diagnosis should not be made primarily on psychometric testing.

The lack of the possibility of paroling these patients is often due to uncontrolled sex urges. The term "selective sterilization" has been introduced, and is applicable to a limited selective field, particularly that of the trained high grade moron.

Progress along this line should be made cautiously. Sterilization as a part of the program is limited to not over 20 per cent of the present institutional population. The state program for the care of the defective includes: (1) examination; (2) registration or census; (3) education, both in school and by formation of special classes; (4) supervision; (5) segregation, and (6) sterilization.

DISCUSSION

DR. EDWARD A. STRECKER: The problem of the feebleminded is much more involved and complicated than can be expressed simply in terms of the intelligence quotient. This country has developed along lines of standardized production and must use the power of the feebleminded for economic purposes. This question may have something to do with industrial unrest and other problems of the nation.

DR. LEROY M. A. MAEDER: Dr. Watkins has mentioned selective sterilization. Sterilization has not met with success in Pennsylvania. One man has made the statement that if all the feebleminded in England were sterilized there would probably be just as many feebleminded in forty years as if sterilization had not been performed. Even feeblemindedness that is hereditary is so widely distributed that one would have to sterilize every one to prevent it. The program includes education. It is known that a good deal of feeblemindedness can be traced back to traumatisms at birth and injuries to the head later in life. Syphilis and various infectious diseases of childhood are also causes. Then, of course, there is a large group of cases due to epidemic encephalitis and other infections. Consequently, there is the program of prophylaxis by prevention of the conditions that lead to feeblemindedness. The third move is institutionalization. The institutionalizing of the woman during the childbearing period is certainly effective in preventing reproduction. It is being attempted to put some of these persons back into the community under group supervision. Social workers are finding out what type of environment feebleminded persons will go back into. They arranged for proper supervision and care. It has been found in New York and in farm and town colonies that the efficiency of the parole system for the feebleminded is directly in proportion to that of the social workers. Therefore, several things are being done: (1) a program of education that begins with physicians; (2) a careful parole system, and (3) institutionalization. Dr. Watkins advises selective sterilization. A bill has been introduced at this session of the legislature, but it has not progressed, because there is much opposition not only by people who have moral and religious scruples, but by physicians who doubt the wisdom of sterilization at this stage.

DR. JAMES J. WAYGOOD: Dr. Maeder emphasizes the need of institutions for the care of feebleminded children, and Dr. Watkins states that there are 6,000 such children in institutions and 100,000 in the community. Feebleminded children are not merely institutional problems. The psychiatrist working in the clinics sees many who will never need institutional care, but who do need special classes and special teachers in the schools, and he finds it very difficult to place these children properly. Certainly, along this line as well, a great deal of missionary work has to be done in the community.

DR. JOHN FISHER: What is being done to prevent the increase in the number of feebleminded and mentally defective persons from growing to even higher proportions? What is your opinion with reference to the feebleminded in public institutions? How many who still carry feebleminded potentials are turned out of the institutions on the strength of acquired improvements, get married and transmit the feebleminded potentials to their offspring?

DR. FREDERIC H. LEAVITT: In reply to Dr. Fisher, I might say that many children are rendered mentally defective at the time of birth as a result of trauma of the brain, and in this respect I believe that the obstetricians can assist materially in reducing the percentage of feeblemindedness. Another means of reducing the percentage is through the mental hygiene movement.

A Comparative Study of Sedatives Employed in Psychoneuroses. Dr. B. P. Weiss.

With the development of new members of the barbituric acid series, pharmacologists naturally began to concern themselves with a study of the relative effectiveness, the toxicity, the rate of elimination and other pharmacologic characteristics of these substances. Contrary to the early erroneous conception that these hypnotics differ only in quantity and not in quality of effect, it is now known that there exist decided differences in their respective therapeutic values. An extensive literature has developed in this field, mainly of a pharmacologic nature, while the clinician has not yet become fully aware of these differences.

Since the beginning of this century, physicians have come into possession of some useful synthetic hypnotics of the barbituric acid series. It has been learned, however, that one must use proper judgment in administering them, and that the barbituric acid compounds, which once were considered to be the last word in hypnotics, are being superseded by safer and more beneficial barbiturates.

In neuropsychiatry, the indications for a sedative-hypnotic are varied, and the therapeutic demands are numerous. Even the best barbiturates, perhaps, do not fit every case. The barbiturates are powerful hypnotics and although, in doses small enough, they can act as sedatives, the transition from mere sedation to hypnotic action is rather abrupt. Yet, in the various forms of excitation that one sees in practice, something is needed that will quiet the patient quickly and for a considerable period without actually putting him to sleep, i. e., a sedative that brings about prolonged sedation but not a quick change to sleep. It is because of these conditions that some of the bromides and other bromine compounds are still used.

Chemistry has again come to the aid of medicine with synthetic sedatives of a milder type than the barbiturates, namely, the ureides. In the clinic with which I am associated, we have recently studied such a "modern type" of sedative allyl-isopropyl-acetyl-carbamide. The chemistry and pharmacology of this new substance, which is a definite chemical compound of crystalline structure, have been described in the literature.

On the basis of these pharmacologic studies and several clinical reports, Demole concludes that allyl-isopropyl-acetyl-carbamide is an unusually safe sedative and a mild hypnotic, which acts in doses far below those that could be considered toxic. While it produces its sedative effect quickly, the state of sedation can be maintained for a longer period, before sleep is desired, than is the case with the barbituric acid hypnotics, which also produce a good sedative effect but soon begin to exert their hypnotic influence. In therapeutic doses, allyl-isopropyl-acetyl-carbamide does not affect circulation or blood pressure, nor does it exert any harmful effect on respiration. No effect is produced on the regulation of body temperature. The substance is completely oxidized in the system and is soon eliminated. Even after large doses, no trace can be found in the urine on the second day. This rapid and definite elimination precludes prolonged effects and cumulation. No albumin, sugar or salt appears in the urine as a consequence of metabolic changes produced by the drug. Neither is the quantity of urine changed.

We decided to submit the new substance to a careful clinical study, and our observations have confirmed the findings described. We may state that the drug is of great therapeutic value in all cases in which one wishes to avoid the use of a powerful barbiturate while, at the same time, a bromide is insufficient. It has been found of service in tiding things over until the etiologic factors could be determined and corrected.

DISCUSSION

Dr. Edward A. Stecker: I doubt very much whether any one has treated patients with neuroses without the use of hypnotic drugs, which should be selected with reference to their efficiency. I wonder how much is known about the hypnotic drugs physicians prescribe, as to their relative toxicity and efficiency. I am horrified at how little I know about the rate of elimination of these drugs. I predict

that Dr. Weiss' discussion will become a clinical paper to turn to before prescribing hypnotic drugs. Allyl-isopropyl-acetyl-carbamide, which all of us have used, stands halfway between bromides and barbital. I may say more than half way, because it has much more power and its action is quicker than the bromides. It produces a long and peaceful sedative effect and has the virtue of producing enough quietude so that psychotherapy will be successful.

DR. BENJAMIN P. WEISS: When the research laboratories of a reputable pharmaceutic house achieve a new drug with the properties that are needed, I think that its benefit justifies its use. In my opinion, allyl-isopropyl-acetyl-carbamide is such a drug, and has earned a place in the list of sedatives employed in the psychoneuroses.

NEW YORK NEUROLOGICAL SOCIETY

Regular Meeting, Oct. 6, 1931

S. PHILIP GOODHART, M.D., *President, in the Chair*

PROGRAM PRESENTED BY THE MEDICAL DEPARTMENT OF YALE UNIVERSITY

A RELEASE PHENOMENON IN ELECTRICAL STIMULATION OF THE "MOTOR" CEREBRAL CORTEX. DR. J. G. DUSSER DE BARENNE and DR. CLYDE MARSHALL.

The procainization of the cortex around a point of the so-called "motor" cortex gives rise, after a latency of from eight to fifteen minutes, to a distinct augmentation of the excitability of this motor point. Not only do the responses of the point become larger with the same liminal stimulus as before the application of procaine hydrochloride, but a spread of responses to other joints of the limb and even to adjacent parts of the body may be observed, together with epileptoid after-discharge in a number of instances. This increase of excitability gradually disappears, so that the initial excitability is restored after from forty-five to sixty minutes following the application of the procaine hydrochloride. The phenomenon was found in cats, dogs and monkeys anesthetized with dial-Ciba.

This cannot be looked on as a facilitation phenomenon in the sense of Exner, Sherrington and Graham Brown, because there were intervals of from one to three minutes between the successive stimulations, and no facilitation was evident before the application of the procaine hydrochloride.

Procainization of a motor point itself invariably gives rise to a distinct diminution or loss of its excitability.

Circumcision of a motor point does not produce the phenomenon described, but results in a long-standing depression or loss of its excitability.

The phenomenon is looked on as a "release phenomenon" in the sense of Hughlings Jackson and Head; the excitability and functional activities of a motor point or a small area of the motor cortex become greater when it is "released" from the influence of the surrounding cortex. In other words, under the conditions of these experiments, and perhaps under normal conditions, the various parts of the motor cortex have a mutual inhibiting influence on each other.

MORPHOGENETIC FACTORS IN THE DEVELOPMENT OF THE CEREBRAL HEMISPHERES. HAROLD S. BURR, PH.D.

In the study of what Dr. Senior has called "long-suffering amphibia," a number of fundamental facts have been unraveled that bear on some of the most intriguing problems of the nervous system. For many years controversy has raged over the

part that environment plays in the organization of biologic systems in general and of the nervous system in particular. The common salamander, Amblystoma punctatum, offers a peculiarly suitable mechanism through which to study that problem. The cerebral hemisphere is almost exclusively an olfactory organ. Nine tenths of its neurons form primary, secondary and tertiary nuclei on the olfactory pathway. The caudal pole alone is concerned with other activities. If, then, the peripheral olfactory mechanism is removed by excision of the primitive placode antecedent to the growth of the olfactory nerve into the central nervous system, a condition is set up in which a part of the central nervous system develops in the absence of the major portion of its normal functional activity. What is the result? From the time of operation up to the point at which the embryo becomes a free swimming form, no longer dependent for its food on the yolk sac, nothing happens. The cerebral hemisphere grows and differentiates in what is apparently a normal fashion. With the beginning of feeding, however, the normal cerebral hemisphere continues to grow, while that deprived of peripheral olfactory systems fails to show the same rate of growth. The result at metamorphosis is a disparity of about one-third between the normal forebrain and that operated on. At first glance this looks as though a functional element were imperative for the complete development of the nervous system. Further analysis, however, nullifies what seems to have been a cleancut result. When the cerebral hemisphere was deprived of its peripheral olfactory connections, two factors in its environment were changed. Not only were incoming olfactory stimuli prevented, but the axons over which those stimuli pass were also removed. Physiologic stimuli failed to reach the primary olfactory centers, so that the growing telodendria of the incoming olfactory nerve were likewise absent from the environment of the primary centers. It is possible, therefore, that ingrowing axons, whether functional or not, might be responsible for the complete development of the hemispheres.

To test this, a second series of experiments was performed which, while not giving a conclusive answer, were suggestive. The entire hemisphere, plus the olfactory placode, was transplanted back on the body of the embryo, in one series with the placode at the surface, in the other with the placode buried deep beneath the surface. In the first series the placode became an olfactory sac open to the exterior, its neurons in a position to be stimulated by changes in the external chemical environment. In the second series, it became a cystic sac without access to the exterior, with little chance of being affected by the external environment. Subsequent examination indicated no observable differences in the hemispheres under the two conditions. While functional activity is not ruled out, in the second series it manifestly cannot be nearly as great as in the first series. These results seem to suggest that the ingrowing axons are potent factors in the organization of the hemisphere. If that is so, the question at once arises, "How potent are these axons"? In this connection, a series of experiments the reverse of the first series was performed. The placode was left intact, but the cerebral hemisphere was removed. To the amazement and consternation of my associates and me, there developed from the curtain of the ependymal cells, which healed the damage to the brain, a new and quite normal hemisphere. The axons from the olfactory placode emerge as factors of prime importance in the organization of the central nervous system. Immediately, a new question arises. What would happen if two olfactory nerves established contact with the hemisphere? This condition is easily realized by transplanting an additional placode adjacent to the normal placode. The results gave a number of interesting answers. In a certain percentage of the cases the additional olfactory nerve joins that of the host and enters the cerebral hemisphere, and, after thousands of cells are counted, hyperplasia of the cerebral hemisphere is found. This is not unlike Dr. Detwiler's findings in his limb transplantation experiments. However, it is just enough different to complicate the problem enormously. In the one instance peripheral overloading produced the hyperplasia without an increase in the number of incoming axons, while in the other the hyperplasia was a direct result of an increased number of telodendria. The olfactory nerve, however, does not always take this

course, but follows Harrison's fundamental principle of stereotropism. It follows the ophthalmic division of the fifth nerve cephalically in some instances and caudally in others, and produces a hyperplasia of the fifth ganglion. But what is even more extraordinary, in a small number of cases, as a result of no apparent factor in the biologic environment, the olfactory nerve enters the dorsal part of the thalamencephalon.

Innumerable questions now arise of which we can consider only a limited number. What factors determine this aberrant path? What happens in the nervous system as a result? What is the significance of such a finding?

To the first question we can give no definite answer. One might read into it "purposive behavior," the attraction of like to like, reversion to a more primitive condition, etc. A much more probable explanation is to be found in the fact that actively growing masses of cells become centers of activity that attract growing axons. Such cell proliferation occurs in Amblystoma, apparently in response to an axial gradient. One of these activities at the time of operation may serve as the directing force.

The second question, What happens? is easy to answer. The fibers enter the pars dorsalis thalami, penetrate to the central gray matter, and there produce hyperplasia of a limited region. There seems to be little doubt that the presence of telodendria in a mass of neuroblasts is sufficient to extend cell division in that area. The significance of this aberrant nerve is of profound interest. There are beginning to be clues as to how neurons take the course that they do through the nervous system. So far as I know this is the first time that it has been demonstrated beyond question that a neuron may establish a wrong connection or at least a different connection within the central nervous system. If it is true that under certain conditions neurons depart from their normal path and establish new ones, what a profound effect that must have on the study of the nervous system, particularly on the handling of the problems of the growing human biologic systems! Nearly all of our experimental work seems to show that environment is a growth factor but not an organizing factor in the nervous system. However, changes in the physiologic or electrical environment of growing neuroblasts produce a completely altered organization.

THE BABINSKI REFLEX IN THE MONKEY, BABOON AND CHIMPANZEE. DR. J. F. FULTON.

In association with Dr. Allen Keller, a systematic study has been made of the conditions necessary for the production of the Babinski reflex (plantar extension with fanning of the toes) in monkeys, baboons and chimpanzees. The investigation incidentally has shed light on the larger problem of the development of pyramidal control in primates, and our general conclusions concerning the evolution of cortical dominance will be set forth when the full text of the paper is published. The more specific observations may be summarized as follows:

Monkeys.—The Babinski reflex did not appear after complete ablation of the motor foot-area in any of the three species of monkeys studied (Macacus rhesus, Cercocebus lunulatus and Erythrocebus). After complete removal of an entire cerebral hemisphere, a primitive defensor reflex can be elicited in the hemiplegic lower extremity, but little or no extension of the toes is seen. Complete lateral semisection of the monkey's spinal cord low in the dorsal region is followed, after from two to three weeks, by a well marked Babinski reflex in the ipsolateral extremity; i. e., it slows plantar extension with fanning of the toes, always associated with generalized flexion of the extremity as a whole. Unless the cord is transected in two stages, the Babinski reflex generally does not appear in the spinal monkey, owing probably to the severity of the spinal shock. Spinal shock in the monkey is associated with extensive degeneration of the motor nerve fibers emerging from the cord below the level of the transection.

Baboons.—Ablation of the foot-area of the baboon (Papio papio) causes a more profound flaccid paralyses than in the monkey, but the knee jerk is not abolished.

Within twenty-four hours after ablation of the foot-area, a primitive Babinski reflex appears, characterized by rapid jerking extension of the toes and generalized flexion of the whole extremity. In the two animals studied the phenomenon has persisted for four months, despite an apparently complete recovery of voluntary power. Generalized flexion of the monoplegic extremity with extension of the toes can be elicited on application of a nociceptive stimulus anywhere on the surface of the body.

Chimpanzees.—Ablation of the foot-area causes a profound flaccid paralysis with abolition of the knee jerk for from twenty-four to forty-eight hours; the state of the spinal centers during the first two days is, in fact, akin to spinal shock. The Babinski reflex appears within from twelve to twenty-four hours after extirpation of the opposite motor foot-area; its characteristics, however, change markedly with time, and the temporal sequence may be divided into three phases: 1. During the first four days, jerking extension of the toes occurs with little movement of the hallux, and the response is overshadowed by generalized flexion of the extremity. 2. From the fifth to the thirtieth day, the extensor movement of the toes becomes progressively slower, with more fanning and greater amplitude of movement and the hallux increasingly abducted; generalized flexion of the extremity gradually diminishes. 3. After the fifth week, a typical Babinski reflex persists unassociated with concomitant contraction of the hip, knee or ankle flexors.

Ablation of the foot-area also causes changes in the plantar responses of the ipsolateral foot. Removal of the second motor foot-area causes the newly paralyzed extremity to lapse into a state of shock lasting five or six days, and a marked change comes about in the resting posture of the ipsolateral toes. It is concluded that the uncrossed pyramidal pathways of the chimpanzee contribute importantly to the control of the ipsolateral foot. The syndrome of the longitudinal sinus is discussed in the light of these observations.

Disorders of the Optic Nystagmus Observed in Lesions of the Frontal Lobe. Dr. James C. Fox, Jr., and Dr. Raymond Dodge.

Electrical stimulation of the second frontal convolution, particularly in its inferior portion just anterior to the precentral gyrus, in animals with binocular vision causes lateral conjugate movements of the eyeballs toward the opposite side. There is no doubt of the existence of this frontal center in man also. A destructive lesion in this region of the brain may cause a transient inability to direct the gaze to the opposite side on command, or there may be difficulty in maintaining ocular deviation to the opposite side. An irritating lesion of this area excites clonic conjugate movements of the eyes to the opposite side.

The rôle played by the frontal "Blickzentrum" in the reflex mechanism governing optic nystagmus has puzzled all investigators in this field. Stenvers was the first to report a case of tumor of the frontal lobe in which optic nystagmus was absent in response to one direction of movement of the visual field and normal to the other direction. This observation has since been confirmed by many others. Fox and Holmes reported a case in which a previously normal optic nystagmus to the left disappeared following two deep operative incisions in the right frontal lobe, one in the anterior part of the third convolution and the second in the posterior end of the second and third gyri. Presumably, the latter wound injured the center, or its connecting pathway just beneath.

Some form of graphic recording device is essential for the analytic and comparative study of the finer details of all types of ocular movements. In our work the nystagmograph has been used; it employs the principle of the photographing of horizontal deviations of the conjugately moving closed eye. A mirror recorder placed against the closed lid of one eye, tangential to the underlying corneal surface, reflects a beam of light to moving photographic paper. The concave surface of a large wire mesh cylinder revolving around the subject's head carries visual objects of desired complexity and frequency.

This report is based on detailed study in five cases with lesions situated in the frontal lobe, the localization of which was determined at operation. In two of the cases optic nystagmus was disturbed when the visual objects were moving in a direction toward the side of the lesion. In the first case, a glioma on the surface between the middle and inferior convolutions and infiltrated deeply into the frontal lobe had been partially extirpated. In the second case, the right frontal lobe had been transected anterior to the precentral gyrus. On the other hand, the nystagmographic records of another patient in whom the right frontal lobe had also been transected at a level somewhat more posteriorly showed no significant alteration of optic nystagmus. Optic nystagmus was also normal to both directions of movement of the visual field in two other cases, one with an extensive hemangioma in the left frontal lobe and another with a metastatic lesion in the right frontal lobe.

In the light of the evidence so far accumulated by various observers it appears that lesions of the frontal lobe vary in their capacity to disturb optic nystagmus. This definite statement can be made: Optic nystagmus is frequently normal and is rarely abolished. When the ocular response is disturbed, the defect always occurs when the visual objects are moving toward the side of the lesion. The volitional eye movement centers in the frontal lobe obviously play a secondary rôle in the reflex mechanism underlying optic nystagmus, as compared with the centers in the paravisual area of the occipital lobe. A lesion in this optomotor field or an interruption of the optomotor pathway — the corticofugal system of the optic radiation — is the primary cause for a defect in optic nystagmus.

AN EXPERIMENTAL STUDY OF THE FUNCTION OF THE FRONTAL LOBES IN DOGS. DR. WILLIAM C. GERMAN, DR. SAMUEL C. HARVEY and DR. LOUIS N. CLAIBORN.

A series of observations was made on the effects of transection of the frontal lobes in dogs. Special emphasis was placed on the study of: (1) retention of recently acquired habits, (2) postural disturbances, (3) changes in temperament and (4) the ability to relearn following operation.

The animals were trained to carry out a series of maneuvers in response to visual and auditory stimuli. The tests were arranged to demonstrate any existing postural defect. The operations were performed in three stages: (1) exposure of the dura covering one frontal lobe; (2) transection of one frontal lobe with the electrocautery, and (3) transection of the remaining frontal lobe. Motion pictures were taken before and after each operative procedure and during the period of relearning.

The results were as follows: Simple craniotomy and transection of one frontal lobe produced no noticeable permanent changes. Transection of both frontal lobes resulted in complete loss of all but the most simple acquired habits. Definite postural disturbances, which were interpreted as being principally a result of spatial disorientation, were observed. For a period of several months there were obvious mental confusion and apparent inability to recognize persons or to respond to any but the simplest commands.

After a period of secondary training the more simple sensorimotor habits were reacquired, but these were performed less accurately than before operation. The more complicated maneuvers were not relearned in spite of a training period of over six months. The inability to reestablish these habits appeared to be due to two factors: (1) the failure to associate the sensory stimulus with the required motor response, and (2) a spatial disorientation, increasing the difficulty of the maneuvers.

DISCUSSION ON PRECEDING PAPERS

DR. J. RAMSAY HUNT: It is a pleasure to participate in this program of representatives of the Yale Medical School, now one of the leading schools of neurophysiology in the country. Neurophysiology is not my special field, so I shall not attempt to discuss these papers in a technical way, but Dr. de Barenne's study of the cortex again brings to the fore the fundamental importance of inhibi-

tion in all phenomena of the central nervous system, a subject in which I have been especially interested. It is known how much stress Pavlov has laid on this in his studies of the conditioned reflex, and it is assuming more and more importance as one of the problems of psychopathology. There are many theories of inhibition, some chemical, some physical and others physiologic in nature. None has been very satisfying to one who approaches the central nervous system from the neuropathologic standpoint. A few years ago, in studies of the pathology of the corpus striatum, I came on a "lead" based on neuropathology that may throw no little light on this obscure question of inhibition.

In the corpus striatum there are two fundamental types of cells. One is the large motor cell, similar to the cells of Betz or the anterior horn cells of the spinal cord. These I have termed pallidal or globus pallidus cells for the reason that the cellular content of the globus pallidus is of this type. In juvenile paralysis agitans, which is a primary system disease (Hunt, J. R.: Primary Atrophy of the Pallidal System, *Brain* **40**:58, 1917), this type of cell undergoes atrophy, and the symptom complex of paralysis agitans results. This point of view has been confirmed by some German and French investigators, and recently by von Bogaert of Antwerp. It is therefore pretty well established that these large cells (Golgi type I) are motor.

The other cells of the striatum are neostriatal. These are small cells which are intraganglionic in origin and termination and belong to the so-called Golgi type II cell. When these cells undergo degeneration, as in Huntington's chorea, chorea results. This correlation has been confirmed by subsequent investigators and is now fairly well established.

In the striatum, therefore, there are two cellular systems related to the two major motor phenomena of this ganglion: (1) the large motor cells, to which paralysis agitans is related, and (2) the small cells to which chorea is related. One represents a paralysis of motion, the other a paralysis of inhibition. The cells of motor type (Golgi type I) elsewhere in the body are all related to motility, e. g., the anterior horn cells of the spinal cord, the motor cells of the rolandic area and the cellular groupings of the cranial nerve nuclei. As the small cells of Golgi type II in the striatum are related to inhibition in this ganglion, it was thought that by analogy it might be assumed that small cells of similar type elsewhere in the central nervous system would have a similar function. I thought that these facts indicated the cellular nature of inhibition — that there is in the central nervous system an inhibitory type of cell, which when destroyed releases motor cells from control. These small cells of Golgi are distributed throughout the gray matter of the central nervous system. They are present in the spinal cord, in the layers of the cortex, where they are very numerous, in the cerebellum and indeed in every ganglionic structure of the central nervous system, and while these cells are very widespread in the central nervous system no definite function has been attached to them as yet. Von Monakow thought that they were association cells because they formed evident communication between neurons; Cajal did not regard them as association cells, but thought that they were condenser cells, admitting that his theory was a purely speculative one. Here then is a cell type, widespread throughout the entire nervous system, to which no positive function has as yet been attached.

In the sympathetic nervous system, Gaskell and Langley have shown that both excitation and inhibition are related to distinct and separate neurons. As the two functions of excitation and inhibition are related to special systems at the vegetative level, it has always seemed to me that nature, in the course of evolution of the central nervous system, would not entirely abandon the inhibitory system, and that there may perhaps be in these inhibitory cells, which are proved to exist in the corpus striatum, an inhibitory mechanism that has been changed to meet the requirements of integration of the central nervous system. It is interesting, and to an extent confirmatory of this point of view, that the Golgi type II cell is not present in the vegetative nervous system, where it is proved that both excitatory and inhibitory fibers exist (Hunt, J. R.: Cellular Theory of Inhibition, ARCH. NEUROL. & PSYCHIAT. **11**:418 [April] 1924).

Dr. Fulton's study of the Babinski reflex in apes is very striking, and appears to throw new light on this important reflex. I have always thought of the Babinski sign in the new-born infant and in children up to 4 or 5 years of age as physiologic, that is, normal. During that period the pyramidal tracts are being myelinated; later, when they are myelinated, the Babinski sign disappears, and there appears the flexion of the normal adult. My impression has been that this was a lower type of response, probably related to the extrapyramidal or paleokinetic system. With the development of the neokinetic or pyramidal system, this response was inhibited, so that it did not appear unless the pyramidal tract was in some way damaged — then it was released. In the monkey and the baboon, both lower types, there is no Babinski response, which, however, is well marked in the chimpanzee. If Dr. Fulton has any explanation for that, I should be glad to hear it.

DR. LOUIS CASAMAJOR: I was interested in Dr. de Barenne's study of the cerebral cortex under procaine hydrochloride. Pharmacologists say that cocaine is a stimulant, and the type of convulsions that follow cocaine poisoning are cortical convulsions. I suppose that cocaine must work on the cortex in much the same way that procaine hydrochloride does. Dr. de Barenne has shown that this can happen when the drug is applied to the cortex alone. He was careful not to draw conclusions as to whether his observations showed the existence of inhibitions in the cerebral cortex. Neurophysiologists have been fighting for years over the question as to whether there is inhibition in nerve action. Dr. de Barenne's study makes one wonder whether the convulsions may not be due to an inhibitory function in nerve tissue. Personally, I do not see how they could come from pure stimulation of any cell unless as a part of the stimulation there was a release of some inhibitory influence from somewhere else. I should like to hear what Dr. de Barenne has to say about that.

I wish I could discuss Dr. Burr's paper. What surgeons of embryonal life do shocks me. They do dreadful things to nerve tissues, which I have always thought of as worthy of more respect, and when they grow noses in the middle of the back and bring out a host of new reactions in the spinal cord, it leaves me confused. All this is getting somewhere, I am sure. An enormous amount of evidence is being amassed. They are going to find out something about nerve tissue; when they do, it will be worth while, but at present their results do not fit in with what I know of nerve tissue.

Dr. Fulton's pictures were extremely good. I was interested in the increase of the Babinski phenomenon when he removed the cortical area of the opposite side. It may signify only what Dr. Fulton said, the cutting of the uncrossed pyramidal fibers that control the ipsolateral foot. Whether those tracts remain uncrossed all the way down and pass ipsolateral to the anterior horn cells or not, I am not certain, or whether this is a new contribution to the knowledge of the Babinski phenomenon. I think that Dr. Fulton has struck on something that is a little more than the function of the uncrossed pyramidal tracts. I think that this is caused by the nature of the Babinski phenomenon itself.

Views on nystagmus have undergone a great change in the last twenty years. Bárány tried to place the cause of nystagmus entirely in the internal ear, and later in the cerebellum, and there were those who tried to use his theories to make a neurologic diagnosis on very few facts. Unfortunately, neurologic diagnosis is essentially complex, and nystagmus has many factors connected with it other than the internal ear. Now Dr. Fox brings in the frontal lobe and complicates the matter still more, with a very welcome complication.

I was wondering as I saw Dr. German's pictures whether the results could be ascribed to the removal of the tissue of the frontal lobe, or whether they could possibly be due to a simple ablation of the sense of smell. That is the dominating sense in the dog, and I wonder whether simple removal of the dominant sense in any animal would be sufficient to abolish the results of his training or his intelligence.

DR. ISRAEL WECHSLER: Regarding the paper of Dr. Fulton, I wish to call attention to the fact that many years ago Dr. Brock and I, in studying dystonia musculorum deformans, expressed the opinion that the Babinski phenomenon is the result of activity not of the pyramidal tract, but of the extrapyramidal pathways; this does not contradict the clinical observation that the extensor reflex is a sign of involvement of the pyramidal tract. Dr. Rabiner came to the same conclusion in a later publication. Obviously, if a given pathway is destroyed any resultant activity cannot be due to that pathway, and therefore must be due to the activity of some other pathway. In view of the fact that removal of the pyramidal tract leaves only the extrapyramidal pathways to function, we thought that the Babinski sign is a release phenomenon.

The suggestion of the rôle of the direct pyramidal tract in the production of the Babinski sign recalls the statement made by Oppenheim many years ago regarding the rare occurrence of the sign in poliomyelitis. Among the various explanations that he offered, one attributed the extensor response to a concomitant lesion of the direct pyramidal tract in the spinal cord.

The composite picture of the lesions that Dr. Fox exhibited showed that the areas of the brain that have to do with conjugate deviation of the eyes were mainly impaired, that is, the frontal and parieto-occipital convolutions. He stated also that the nystagmus was abolished on looking to the side of the lesion. Now, that is exactly what happens with the conjugate ocular movements if the cortex is destroyed; that is, the patient cannot look to the side of the lesion. This is the opposite of what happens in positive lesions. I wonder, therefore, whether the loss of nystagmus to which Dr. Fox called attention was not really the result of impairment or loss of conjugate ocular movements.

DR. ARMANDO FERRARO: Dr. de Barenne has reported that following the application of procaine hydrochloride around a certain motor point an increased excitability of this surrounded motor point follows, and that there is besides a spreading of the impulse to other groups of muscles, apparently not governed by the particular group under stimulation. On the other hand, the isolation of the center in question from the surrounding areas by means of the knife would not elicit this increased excitability. It seems to me that in consequence the use of the word "release" by Dr. de Barenne might not explain the whole situation.

In regard to Dr. Fulton's paper, the only thing I can say is a confirmation of the absence of the Babinski sign following the removal of the motor areas in monkeys (Macacus rhesus). Dr. Barrera and I have been operating on a large series of monkeys. I agree with Dr. Casamajor that the appearance of new phenomena following bilateral operation might not be only a question of summation of the removal of the same type of fibers, but that something else, which at the present time is not clear, takes place in the bilateral removals.

DR. J. G. D. DE BARENNE: I tried to be as prudent as possible in giving a name to this observation, and therefore called it a release phenomenon, in order to say as little as possible. Perhaps one may look on it as a release from inhibition by the surrounding cortex, but it may be that after all this is saying too much. It would be very important, of course, to find exactly which cells in the cortex were procainized, but I cannot say anything definite about that. The procaine hydrochloride was colored blue with toluidine blue, and cross-sections of the cortex were made; in a few experiments the blue dye had penetrated only as far as about the fourth superficial layer, leaving uncolored the fifth and sixth layers, in which the large pyramidal Betz cells lie. One might ask whether the procaine hydrochloride diffuses as far, or perhaps farther, than the toluidine blue, and nobody can say with certainty whether that is true. To get an answer to that question, I tried a few experiments.

For the local application of strychnine it is fairly well demonstrated that the strychnine does not diffuse farther than the toluidine blue colored area. Now, in applying first strychnine on part of the dorsal surface of a spinal segment and then procaine hydrochloride on the same area, but within the boundaries of the strychninized area, one can observe that the strychnine syndrome (enormous

hyperesthesia and hyperalgesia of the skin) still persists, only to be extinguished when the areas of strychninization and subsequent procainization are exactly the same. An analogous experiment was done with the same result on the cerebral cortex of the monkey.

These experiments, if they do not prove it, at least indicate that the procaine hydrochloride does not appreciably diffuse beyond the area that is colored blue.

In other experiments, however, it was found that the color of the toluidine blue had penetrated into the white matter, so that probably in these cases also the fifth and sixth cortical layers had come into touch with the procaine.

With regard to Dr. Ferraro's discussion, I might say that we must not look on the cortical reactions by electrical stimulation as definitely fixed reactions, because it is well known, especially through the observations of Graham Brown and Sherrington, that a point at the motor cortex, for instance a motor point of the arm area, which on excitation primarily yields flexion of a joint, may give rise to an extension of this same joint following the excitation of another "extension" point of the adjacent cortex. One also occasionally observes that a motor point may yield movements of one limb, e. g., of the arm one moment, and of the face or of the leg at another time. Therefore one must not look on the subdivisions as established by electrical stimulation of the cortex as absolutely strict divisions and on the cortical reactions as rigid patterns.

From these facts, the spread of reaction elicited from a motor point after procainization of the surrounding cortex may be understood to some extent, but I agree that a satisfactory explanation is rather difficult as yet.

To answer Dr. Casamajor, I might say that, so far as I can see, we have not to do in these experiments with convulsive effects of the procaine as such, because, as I said before, on application of procaine to a motor point of the cortex one invariably finds a diminution, usually a loss, of the excitability of the cortex, so that the direct effect is always on the negative side, and never toward augmentation.

Dr. J. F. Fulton: I wish to mention one thing in Dr. Ramsay Hunt's extraordinarily suggestive discussion, namely, the point that small cells in the nervous system appear to be the inhibitory cells; favoring that assumption is the important fact that on the sensory side of the reflex arc the small fibers are apparently the inhibitors — not only the small medullated fibers but, as Ranson has shown, the small nonmedullated fibers, for both groups mediate pain. They remain small even after entering the central nervous system. Since their ultimate effect is one primarily of inhibition, particularly of the extensor muscle groups, it would be extremely interesting if it proved that in the higher regions of the nervous system inhibition still remains associated with small cells. In mentioning this point, however, I am afraid that I am intruding on another problem.

With reference to the Babinski response, it was suggested that removal of the second foot-area may have some effect that is not associated entirely with the pyramidal system. I am not certain about this, but as far as the direct pyramidals are concerned, it is scarcely true to say, as Kölliker did, that they are merely ipsolateral fibers which ultimately cross at a lower level of the spinal cord. Lewandowsky was convinced that he had seen these fibers terminating on the anterior horn cells, as far down as the fourth lumbar segment in the human being. Undoubtedly a certain number of uncrossed pyramidal fibers do terminate on the anterior horn cells or on internuncial cells that impinge ultimately on the anterior horn cells of the ipsolateral side. I cannot shed any further light on the point that Dr. Hunt mentioned as to the extensor response of the toes being probably a more primitive response than flexion; one must remember that flexion is the reaction that one sees in the first few days after complete transection of the spinal cord in man. Why the extensor response comes on later is a matter of speculation.

Dr. James C. Fox: In reply to Dr. Wechsler's question regarding the presence of a weakness or defect of voluntary conjugate deviation to the opposite side of the lesion in these cases, I may say that the majority of these patients did show

such a disturbance, and we have photographic records of the movements of the eye, both in response to eccentric retinal stimulation and in response to the command, "Look to the right, look to the left." I did not mention this important aspect of the study, but it is only by analysis and comparison of a large group of such records from frontal lesions and by comparing them with the similar types of ocular movements of normal subjects that we can eventually understand fully the rôle of the slow and quick phases in optic nystagmus.

DR. W. C. GERMAN: Regarding the part that ablation of the olfactory lobe plays in the behavior of these animals, it is obvious that the olfactory sense is highly developed in the dog, and he is very dependent on it. However, it is difficult to explain the loss of well formed habits merely by the loss of olfactory sense, and it would appear more logical to assume that this loss of habits was rather dependent on the ablation of the frontal lobe itself. If it were granted that the habits were well formed, and that they were lost because of the ablation of the olfactory lobes, the incorrect inference might be drawn that the actual habit formation was a function of the olfactory lobes.

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DR. W. J. BERNIS, ROCHESTER, N. Y., *Abstractor*

(Concluded from p. 752)

DISTURBANCES OF THE REFLEXES IN CONCUSSION OF THE CENTRAL NERVOUS SYSTEM. DR. F. KINO, Frankfort-on-Main.

Changes in the reflexes following trauma of the central nervous system were first described by Cassirer. Similar observations were made by Aschaffenburg, Redlich, Karplus, Marburg and Foerster. In the type of cases that occurred during the World War and in those caused by violence, in addition to the disturbance of the reflexes there are also motor or sensory disturbances, which partly remain permanent. The disturbances of the reflexes are said to be permanent.

Most of the cases observed by Kino were uncomplicated cases of concussion of the brain; the majority were simple cases, without the slightest sign of any objective or subjective cord involvement. The main group of pure commotio were cases showing rapidly passing symptoms of concussion of the brain and never any indication of essential anatomic injury of the brain or the cord. In this group most cases came under observation not later than eight days after the injury took place. Of one hundred and fifty of the cases, twenty showed changes in the reflexes.

As a rule, the changes are observed in the knee and achilles reflexes, the latter being more often involved, while those of the upper extremities remained unchanged. A symmetrical distribution of the disturbances was found to be more common than a unilateral distribution. The activity of one reflex is independent of the activity of another, so that with the loss of the achilles reflex the patellar reflex may remain normal.

That the injury was the cause of the disturbance of the reflexes is proved by the gradual return of the reflexes to normal activity. The recovery was gradual, but occasionally was subjected to fluctuations. Occasionally, before recovery there was a short phase of increase in the reflexes.

A severe reflex disturbance may follow a relatively mild commotio. The degree of reflex disturbance does not depend on the intensity of the injury. A severe con-

cussion of the brain may show no abnormal changes in the reflexes, although more often they are present.

In contusion of the brain and fracture of the skull the disturbance of the reflexes was found to be about the same as in mild concussion, except as there may be a difference between the right and the left side owing to pyramidal disturbances.

In considering the pathogenesis, Kino was of the opinion that the clinical and the experimental findings indicate that in the mild cases of commotio there is a shaking up of the cord. It must be admitted that concussion of the cord may pass through many grades and that the reflex disturbances, as already mentioned, are to be considered as an expression of a mild form of this condition.

This temporary abnormal action of the tendon reflexes in traumatic injury of the cord can be compared to the transitory manifestations observed in concussion of the brain or of the medulla.

Kino was of the opinion that the relatively short time for recovery in his cases indicated that a real restitution took place.

Whatever histologic investigation may establish in the future, clinically it remains undisputed that even in the mildest shaking up of the central nervous system reflex disturbances are present.

THE PRINCIPLE OF RESTITUTION IN THE BRAIN. DR. NIESSL VON MAYENDORF, Leipzig.

The restoration of a brain function will depend, above all, on whether there is a definite anatomic structure for it, destruction of which stops the function, or whether an entirely different tissue structure is capable of performing this function. In the first case restitution will be impossible, since the same tissue is not replaced; in the second case restitution will be possible, even though limited to a certain extent. The principle of restitution is the rule that decides the measure of this limitation, especially the law that controls the biologic function of a functional transformation. Of whatever kind the nerve current may be, whether of a physical or of a chemical nature, or whether it represents a physicochemical agent, it undoubtedly is concerned with a continuous process in a definite direction. This course depends on the minimal resistance of the route. The visual rays are the direct conduction path of the retina to the brain. The same is true for the pyramidal tracts, which form the route between the brain cortex and the motor nuclei of the cord. The disturbance in the transmission of nerve stimuli may be compared with the flowing of water, which avoids a blockade and takes a roundabout course. Similarly, the nerve impulse always moves forward when the conducting tubes are not interrupted by a group of cells inserted in its route. The return of a function therefore regularly takes the routes that offer the least resistance.

FUNCTIONAL CHANGES IN DISTURBANCES OF SPATIAL FUNCTIONS IN PERCEPTION AND MOVEMENT. DR. VON WEIZSÄCKER, Heidelberg.

The previously described syndrome of systematic disturbances in the motor and optic space perception has been observed and studied in a number of new cases. It was found that in the affected sensory spheres there is a fixed breaking up, in the sense of functional changes. Thus, in the optic sphere there are: a diminution of the fusion frequency of successive stimuli, breaking up of color perception from blindness for red-green up to monochromasy, increased movement of the after-images, contraction of the size of objects (micropsia), a "spiral" field of vision, Palfrich's phenomenon in involvement of one eye, etc. In the tactile sphere there are: a considerable underestimation of objects felt, mistakes in weights, increased fusion of successive stimuli, etc. Thus it can be considered as certain that it is a question of a fixed comprehensible breaking up of function of a formal kind in the sense of sluggishly coursing stimuli. It is questioned whether the

totality and the systematic disturbances of spatial type can also be accounted for by such functional change. A summary of the observations together with those by Goldstein and Reichmann and by Schilder leads to a similar grouping, but of differentiated forms of the breaking up of the function, more or less according to the organ spheres; this is characterized less by "focal symptoms" than through the type of function.

THE INFLUENCE OF STIMULATION OF THE HYPOTHALAMUS ON THE ACTIVITY OF THE HYPOPHYSIS. DR. I. P. KARPLUS and DR. O. PECZENIK.

After stimulation of the hypothalamus the cerebrospinal fluid shows a change in biologic characteristics: The pituitrin-like effect of the fluid on the guinea-pig uterus is increased. This change is due to a pouring out of pituitrin as a result of the stimulation. It was also found that this outpouring of pituitrin does not depend on stimulation of the cervical sympathetic or on a general stimulation of the animal, but that it is the direct result of the stimulation of the hypothalamus. It was shown also that the increase in the pituitrin is not secondary; it does not come from the blood. Apparently the hypothalamus possesses a hormone that regulates the mechanism of the hypophysis.

THE PATHOLOGIC ANATOMY IN EPILEPSY. DR. M. MINKOWSKI, Zurich, Switzerland.

The study concerns changes found in the inferior olive in the medulla, which the author found in seven of ten cases of epilepsy that he investigated.

Older authors long ago maintained that in epilepsy the disturbance is to be found in the cord. Schröder von der Kolk described changes in the brains of persons with epilepsy: a reddening of the fourth ventricle, dilatation of the blood vessels, mostly of the capillaries, of the medulla oblongata, especially in the area of the roots of the hypoglossus and vagus, and thickening of the vascular walls. He also mentioned hyperemia, in the milder cases limiting itself to the dorsal part of the medulla and reaching up to the olives in which there were often found dilated and thickened blood vessels.

Obersteiner has pointed out that even in the normal brain the cells of the olive contain a certain amount of lipoid pigment, which increases with age. Many authors recently have described senile changes in the olive. Von Braunmühl (1928) described a high grade of pigment atrophy in the ganglion cells, breaking up of cells, different types of glial reaction and the formation of glial proliferation and sclerosis as an end-effect. There were also degenerative changes in the nucleus dentatus.

Changes in the olive have repeatedly been described in Parkinson's disease, in the form of swelling, chromatolysis and nuclear accumulation in the ganglion cells and reactive manifestations in the glia in a large number of cases of encephalitis epidemica, in three cases of tetanus and in animals poisoned with barbital. Similar changes have been described in the senium, and also in different infectious diseases, as in sepsis, tuberculous meningitis, typhoid and delirium tremens, and in schizophrenia.

Among the ten cases of different kinds investigated by Minkowski, in patients of different ages, there were four cases of epilepsy and one of eclampsia with positive changes in the olive, in which the patients died in status epilepticus or during an attack, without any intercurrent disease. In these cases the changes in the olive revealed a greater or less similarity to those in the same organ in epilepsy.

Briefly, the changes are: In the olive they represent different stages of a unified progressive pathologic process. The milder and apparently earliest type shows an increase of pigment in the ganglion cells of the olive, which normally is found in adults. Together with this there is present in the same location a progressive dissolution of the tigroid bodies (chromatolysis). In more progressive

stages the nucleus has moved to the periphery of the cell; then it begins to become deformed and stains badly; the plasma is changed more and more into a homogeneous yellowish (lipoid-containing) mass, which often is of balloon shape. In a later stage the latter also tends to disappear; the cell loses all its constituent parts; it continues to shrink more and more, finally disappears and is absorbed, leaving here and there cell débris with areas showing loss of cells or presenting different stages of edema. Summing up, it can be said that there is present a chronic degenerative process in the parenchyma of the olive which begins with pigment degeneration, as a fatty degeneration of the ganglion cells; in a later stage there are pigment atrophy, homogeneous degeneration and sclerosis up to complete disappearance of a part of the nerve cell elements, whereby different stages of the process in different areas can be observed.

The neuroglia partakes in the degenerative process. In the early stages there is proliferation. Elements with vesicular, chromatin-rich nuclei and increased plasma appear in large number; there are also rod-shaped cells with visible protoplasmic processes (which apparently represent activated Hortega cells), and gitter cells containing some fat pigments. Regressive processes are observed at the same time; the nuclei become deformed; some become pale and others become darker and homogeneous; the plasma shrinks and apparently some elements are lost. In older chronic cases, there are areas in which the ganglion cells have either entirely or almost disappeared, and the glia nuclei are sparse. Real neuronophagia is rare.

As to localization, any part of the olive may be involved or the entire organ may be beset with the process; yet this rarely takes place and usually there are areas of predilection and others of maximal ability to resist. The dorsal plate of the olivary gray, the fibrae arcuatae and the entire oral end appear generally to be especially vulnerable. There are variations from case to case. The affected areas are not necessarily connected. The accessory olives, especially the ventral plate and more so the ventral medial part, are more resistant. The process usually extends to both olives.

The medullary part of the olive likewise shows a dilatation and an intensity of the process in the gray band.

The large blood vessels at the base of the medulla show no essential changes; the smaller blood vessels within and around the olive, especially in the part where the degenerative process is in its early stage, show more or less an infiltration of the perivascular spaces with different kinds of cells, nominally of the character of phagocytic cells, which are partly loaded with pigments. The walls of the blood vessels are thickened; other small precapillary blood vessels within the degenerated area are unusually thin. In older cases of epilepsy, in which the degeneration of the olive is far advanced, the blood vessels are found in a less active stage. Hemorrhages within and around the degenerated lesion are seldom observed.

In the cerebellum, the hemispheres, the vermis and the nuclei show here and there different changes, but these are not extensive.

Of two other cases of epilepsy with changes in the olive, one was combined with other diseases, so that the conclusion from the observations was not entirely clear. Even then consideration must be given to the changes in the olive, at least as a contributory factor of epilepsy.

Against the seven cases of epilepsy with changes in the olives, Minkowski found three cases in which the olives were essentially normal.

Thirteen control cases that had no connection with epilepsy were observed. In general, it must be said that in the adult there is always more or less fatty change in the ganglion cells of the medulla, while in the child this is absent. However, a condition like that found in epilepsy is not frequently observed. In the thirteen cases there were only four that showed considerable changes, such as pigment atrophy, homogeneity and breaking up and disappearance of ganglion cells, with corresponding gliosis and involvement of the blood vessels.

On the basis of the observation cited, Minkowski feels justified in reaching the conclusion that the inferior olive represents a vulnerable organ which is

affected by different diseases. This is true not only for the senium, Parkinson's disease, intoxications and different acute and chronic infectious diseases, such as epidemic encephalitis, dementia paralytica, pneumonia, etc., but especially also for epilepsy and for diseases that go together with epileptic attacks and in which similar changes in the inferior olive are often found. At the same time it is instructive to observe how different noxae may bring about a similar pathologic process.

The changes in the olive in cases of epilepsy and in different other diseases recall the well known sclerosis in the cornu ammonis, which is likewise found not only in cases of epilepsy but also in the senium, in dementia paralytica and in other diseases.

In evaluating the relation of these observations to epilepsy, Minkowski cannot say that they represent a primary cause of epilepsy. Against it, aside from other reasons, speaks especially the fact that negative cases were found. Minkowski is inclined rather to think that it is a special pathologico-anatomic expression either of the attacks themselves or of the processes responsible for the attacks, perhaps a combination of the two, affecting a structure that is very sensitive, such as the olive. The latter conception appears to Minkowski to be the most plausible.

Minkowski is of the opinion that the degeneration in the olive, on which Spielmeyer generally lays such stress, and the changes in the cornu ammonis and cerebellum in epilepsy need further proof. His own investigations do not support this view. The blood vessels in and around the degenerated areas of the olive indeed show changes in the form of moderate proliferation and thickening of the walls and more or less intensive infiltration of the perivascular spaces. Nevertheless, it is partly the result of reactive processes conditioned by the breaking up of nerve parenchyma, and also, in part, of causes bringing about vascular alterations such as are often found in other parts of the medulla and other places. Furthermore, no closer connection can be established between the localization of vascular alterations in the medulla and the degenerative processes in the olive. As a matter of fact, Spielmeyer considered that the pathologic changes in the cornu ammonis and in the cerebellum in epilepsy were caused by angiospastic conditions. But this standpoint is not sufficient to explain the degenerative process in the olive. In fact, so far as location is concerned, the lesions not only vary from case to case but in this respect even show considerable differences between the two sides. Furthermore, the histologic processes in the cells themselves generally do not present the picture of ischemic cell disease, as it is observed in angiospasm, but rather a pigment atrophy and a homogeneous cell disease. Even if the importance of the circulatory disturbance in bringing about the degeneration of the olive were not questioned, it would then at least take in other areas. The fact that both accessory olives, and in the olive itself the ventromedial part and the oral pole, show special resistance would tend to indicate that with reference to local selection of the degenerative process developmental systematic factors also play a part, since these parts, according to Brouwer and Rudolf Brun, belong to the paleo-olive and are connected with the paleocerebellum. At any rate, to explain the frequency of the degeneration of the olive in the different diseases and especially in epilepsy, in addition to a general systemic factor, a great deal of consideration must be given to inherited qualities of the organ, developmental anomalies and other endogenous and exogenous factors, which individually require further study.

THE PROBLEM OF ENCEPHALOMYELITIS AND MULTIPLE SCLEROSIS. DR. J. GERSTMANN and DR. E. STRAÜSSLER, Vienna, Austria.

This paper is based on the report of two cases of meningo-encephalomyelitis, and discusses first the relation to multiple sclerosis and then the relation between the clinical picture and the histopathologic observations.

The first case is that of a woman, aged 60, whose illness had lasted seven months. During the last two months, she suffered from attacks of tonic fits,

partly local and partly generalized, while consciousness was maintained. The attacks of fits often followed sensory and psychic stimulation.

Other observations were: tension of the muscles of the extremities, mainly of an extrapyramidal character; pain in the extremities of a central nature, which greatly increased in severity during a fit; diminished motor power and motility of the lower extremities; increased deep reflexes; a Babinski sign on the right; occasional rest tremor, and arteriosclerosis of the retinal blood vessels.

Death occurred as a result of cystopyelitis. From the clinical picture the diagnosis was a lesion in the inter-midbrain, due to either encephalitis or arteriosclerosis.

The histologic picture corresponded remarkably well with a so-called transitional case between meningo-encephalomyelitis and multiple sclerosis. The entire central nervous system was covered with diffused inflammation, and was infiltrated with lymphocytes and plasma cells, which everywhere preferred the white substance, caudally increasing in intensity, while the interbrain and midbrain were not more involved than the adjacent regions; along the entire cord there was a marked increase in the intensity of the process.

In addition, there were disseminated lesions in the cord with many sclerotic plaques, more in the middle cervical and upper dorsal regions. In the sixth cervical segment, in the region of the posterolateral columns, including a part of the posterior horn, a lesion was found that resembled exactly that of multiple sclerosis. The same section, however, showed also, in the anterior and posterior columns, demyelinization that differed from typical multiple sclerosis by the lack of a sharp delimitation.

The lesion in the lateral column was in every way that of a chronic multiple sclerosis. Other lesions, as in the fourth cervical, were marked by a considerable proliferation around the blood vessels. The resultant process of the glial proliferation assumed mostly an anisomorphous character. The axis-cylinders showed a remarkable resistance. In some places the lesions showed softening and confluence of the tissue.

The authors are unable to decide whether to designate this case as one of multiple sclerosis. Aside from the rarity of histologic manifestations in multiple sclerosis, such as connective tissue proliferation, hemorrhage, softening and an anisomorphous character of glial proliferation, the clinical symptoms were scarcely those of multiple sclerosis. Until further light is thrown on the subject, the authors lean to the opinion that encephalomyelitis diffusa may show lesions that closely resemble multiple sclerosis.

A comparison between the clinical symptoms and the histopathologic observations in this case discloses a remarkable dissociation between them. In the former there is a complex of manifestations pointing to a lesion, circumscribed in the inter-midbrain area, while examination reveals an extensive diffused process over the entire central nervous system, with an intensity of lesions in other areas.

The second case was that of a woman, aged 27, who for seven years had had intermittent attacks of purely motor disturbances involving the cranial nerves and the extremities (ocular muscle palsy, atrophy and paresis of the tongue, weakness of the soft palate, disturbance of swallowing, bulbar speech, double facial paresis, paresis of the upper and lower extremities, with muscular atrophy in the former, increased deep reflexes and a double Babinski sign). A diagnosis of encephalomyelitis disseminata, with predilection for the motor cranial nerves, was made.

The pathologic observations were those of a mild grade of diffused encephalomyelitis, which involved mainly the white substance, with no local accentuation. Although the gray substance was not absolutely free from the inflammatory process, the nuclei in the brain stem, as well as the corresponding sections from the medulla and midbrain or from the cervical cord, showed no such changes to account in the remotest way for the clinical symptoms.

If in the first case the dissociation between the clinical picture and the histopathologic condition consisted in that in a high grade encephalomyelitis a localized lesion brought on a symptom complex without a corresponding histopathologic

correlation, in the second case it consisted in that a similar diffused, but milder, grade of encephalitis brought about a system type of disease.

Both cases show conclusively that the essence of encephalomyelitic disease processes appears not to be exhausted by the morphologic observations.

A Cerebellar Symptom. Dr. R. Wartenberg, Freiburg-in-Breisgau.

A girl, aged 12, for three months complained of headaches and vomiting. Examination disclosed a pressure pulse, choked disks, nystagmus with a larger amplitude to the right, a slight right adiadokokinesis, a fine intention tremor in the right hand and uncertainty of gait with a stronger tendency to fall to the right. A diagnosis was made of a tumor in the posterior fossa, and most likely in the right upper hemisphere. A tumor the size of a hazel nut (a fibrosarcoma) was radically enucleated from the middle of the right cerebellar hemisphere. Four months after the operation, all the symptoms had entirely disappeared.

The importance of this case lies in the fact that before the operation the right arm showed no pendulum movement in walking and returned to normal after the operation. It is to be observed that in the right arm there were no indications of pyramidal or extrapyramidal disturbances, and that the cerebellar symptoms were not very marked.

Other cases of cerebellar lesions were then observed, and in every case there was found a weakness of the pendulum movements of the arm in walking. Of interest is a case with the symptom complex of a tumor of the right cerebellar lower surface. The pendulum movement of the right arm in walking was decidedly weakened. Under treatment with iodine and roentgen radiations (or spontaneously) the symptoms largely disappeared and the pendulum movement of the right arm in walking again returned to normal. On the other hand, in a case of tumor of the vermis, verified post mortem, the pendulum movements were normal on both sides.

This symptom is not new. It has been mentioned by Goldstein, Marburg, Dusser de Barenne, André-Thomas and Gordon Holmes. It is of diagnostic importance as an early symptom.

Experimental Poliomyelitis. Dr. H. Demme, Hamburg-Eppendorf.

Experimental poliomyelitis in the monkey presents a true picture of poliomyelitis as observed in man, and thus permits conclusions of considerable importance as to its relations in man. The course of poliomyelitis and its anatomic substratum in human beings in the different stages of paralysis are comparatively well known. Animal experiments, however, permit not only an anatomic investigation at each stage of the disease, but also careful study of the disease in the preparalytic stage, when clinical symptoms are not yet present.

The material used was a virus (cord emulsion) from a monkey that had died of poliomyelitis, obtained from Professor Kling in Stockholm. The virus had been cultivated for fifteen years, and was very virulent for the monkey, killing nearly 100 per cent of the animals in a few days. The injections were mainly intraneural (median, sciatic or facial). In some animals the injections were made into the mucous membrane (of the nose or the stomach) and into the blood. In addition to careful clinical observations, the temperature was taken, and examinations of the blood and spinal fluid were made. Microscopic and culture proofs of the virus (Flexner) for technical reasons were not undertaken.

The incubation period in the animals experimented on varied according to the different methods of inoculation. If the incubation period is figured from the time of inoculation to the time of the first appearance of paralytic manifestations, the shortest period was from intravenous inoculation in the lower leg. In two animals, as early as twenty-four hours after the inoculation the gait became unsteady and a tremor of the entire body developed. On the following day there were definite manifestations of paralysis.

With intraneural inoculation the incubation period was the shortest, as the incubation area was nearer to the central nervous system: three days with a facial inoculation, and considerably longer (seven days) with an intercerebral inoculation. The longest incubation period was from inoculation of the mucous membrane.

Mode of Inoculation	Incubation Period, Days
Intravenous	2
Facial nerve	3
Median nerve	4-6
Sciatic nerve	5
Cerebral	7
Nose	10
Stomach	14

While the animals inoculated in the peripheral nerves always showed the first paralytic manifestations in the inoculated extremity, the monkeys inoculated intravenously showed first general manifestations (tremor, unsteadiness and weakness). The spreading of the virus in the organism in poliomyelitis differs from that of tetanus toxin. With tetanus toxin the disease develops more rapidly when it is inoculated by the nerve route, while in poliomyelitis the process develops more rapidly when the infection is by the vascular route.

Demme is unable to state whether, after inoculation of the mucous membrane, the extension of the virus takes place by the vascular, lymphatic or the nervous route. The observation is important that so far infection succeeded only when the mucous membrane was injured. When the virus is rubbed in the nose the mucous membrane is injured, and small hemorrhages may take place. Two animals were inoculated by means of a stomach tube. In one, several days before the inoculation, saponin was given with the food. The second animal was not similarly prepared. Poliomyelitis developed in the first animal, but the second remained well. These observations are of practical importance because in human beings the paralysis is often preceded by an infectious fever which is diagnosed as angina, bronchitis, intestinal grip, etc. In a few days, with the disappearance of the infection, the temperature falls to normal and the poliomyelitis begins to manifest itself, at first with general manifestations, fever, headaches and general weakness; soon after this, paralysis occurs. Whether the disease condition preceding poliomyelitis is the first symptom of poliomyelitis itself or whether it is an entirely independent disease, which permits the poliomyelitis virus an entrance in the organism, must at present remain unanswered. Demme's experiments favor the latter view.

This question becomes more difficult to answer since the general symptoms in the experimental animal are more difficult to observe. The temperature curve leads to no definite conclusions, since normally the temperature of experimental animals is subject to considerable changes.

Regarding the general reaction, the blood picture is of some importance. Some investigators frequently observed in human poliomyelitis a leukopenia; others, a leukocytosis. In poliomyelitis of the monkey, Taylor found during the incubation period nearly a normal leukocyte count with a moderate lymphopenia; during the acute stage the number of lymphocytes further decreased, and at the same time the leukocytes increased. Demme's experiments to a certain extent contradict Taylor's observations. Demme found soon after incubation, at any rate as early as in the preparalytic stage, a marked increase in the leukocytes with the percentage of the different elements varying but slightly.

More interesting were the changes in the cerebrospinal fluid, which was regularly examined; in some cases daily punctures were made. The spinal fluid of all animals was carefully examined before they were subjected to experiments, and only healthy animals were used. Control experiments were instituted also, with the object of finding out whether the mere removal of the fluid as such acts as an irritant that is capable of producing a pleocytosis in the fluid. It was found that the removal of a large quantity of fluid did so; it is impossible to prevent the

entrance of air into the fluid space after the removal of from 1 to 1.5 cc. of fluid from the cisterna. This "irritation pleocytosis" is capable of increasing the cell count to 100/3; usually it is below this number; it seldom reaches the high mark observed after infection with poliomyelitis. Then again, after a few days the cells disappear. Even when blood finds its way into the fluid space during the puncture, the cells may increase to the number of 100/3 during the following days.

Demme in his experiments limited the removal of the fluid to a few drops; therefore, he could make only a cell count; in a few experiments the mastic reaction was obtained also.

In animals inoculated in a peripheral nerve the pleocytosis in the fluid always appeared very early. It appeared earliest when the facial nerve was inoculated. After twenty-four hours, this animal showed 420/3 cells in the fluid, which did not contain poliomyelitis virus; the animals inoculated with the fluid remained well. The first clinical manifestations in the monkeys inoculated in the facial nerve appeared two days after the appearance of a pleocytosis in the fluid, that is, three days after the inoculation.

As already mentioned, the virus employed was very virulent. Up to the time of death, the cells kept on increasing in number and usually reached 1,000/3. In three cases only did the number decrease again.

The cells were largely lymphocytes; one third of all the cells were polymorphonuclear. In most of the cases there was a considerable pleocytosis in the fluid one or two days before paralytic symptoms appeared. This observation should be of some importance in the early diagnosis of poliomyelitis. It indicates that when the first paralytic manifestations appear there may already be marked changes in the central nervous system. The disappearance of the inflammatory reaction in the fluid could not be observed with this virulent stock. Experiments with a less virulent stock, which could not be further transferred, showed a slower increase of the cells in the fluid. Here, too, the pleocytosis appeared three days before paralysis set in.

It is noticeable that in cases in which the increased leukocytosis in the blood ran parallel with the cellular condition in the fluid, there was agreement between the leukocytosis in the blood and the pleocytosis in the fluid.

As regards immunization experiments, Demme can at present offer no conclusions. His observations, however, especially his studies of the blood and cerebrospinal fluid, speak in the sense that long before the appearance of paralysis there is a strong defensive reaction not only of the central nervous system but also of the entire organism, that is, long before the disease picture appears as a poliomyelitis. Immunization therapy employed after the appearance of paralysis is too late.

EXPERIMENTAL POLIOMYELITIS. DR. H. PETTE, Magdeburg.

In acute infections of the central nervous system involving mainly the gray matter it is characteristic that the symptoms come on acutely and within a limited space of time. Especially is this true of poliomyelitis. Human pathology does not generally permit the right conception of the process in its particular phases. Animal experimentation is indispensable. But even animal experimentation can bring clarification only when the clinician, biologist, serologist and anatomist work together.

In a study of the histologic processes Pette observed the development and the disappearance as well as the extension of the process. The earliest changes that Pette found in an animal inoculated through the median nerve was in one that was killed three days later. In one of the spinal ganglia belonging to the median nerve the amphicytes were strongly increased in the absence of any mesodermal reaction, as well as of any disease change in the parenchyma of the cord. Shortly before death, the monkey had a pleocytosis of 2,240/3. This apparent discrepancy between the serologic and histologic observations deserves special con-

sideration with reference to the development of the process during the so-called preparalytic stage of poliomyelitis. So far, from his studies Pette cannot express a definite opinion.

In neural inoculation the virus travels by way of the peripheral nerve, spinal ganglion and roots into the cord. With the appearance of paralytic manifestations the recognizable histologic process is no longer limited to appertaining peripheral segments. By this time the process has more or less spread even to distant areas, although it is always observed that the centers belonging to the inoculated area are more strongly involved.

The process is recognized as such, first by the changes in the parenchyma, specifically in the ganglion cells, and then by the mesodermal and glial reaction.

The ganglion cells show changes of different grades, beginning with simple swelling with tigrolysis and vacuole formation up to the severe cell change of Nissl. In addition, during the early paralytic stage there are observed a number of ganglion cells undergoing leukocytic neuronophagia, either partially or completely. Soon after, the leukocytes are replaced by lymphocytes and glial (Hortega's) elements. Glial neuronophagia may take place. At times, even in severe cases, among all this there are also observed normal ganglion cells with well retained Nissl bodies.

The leukocytic reaction is the direct result of the effect of the virus on the parenchyma and primarily on the ganglion cells. The leukocytes invade more or less the tissue near the ganglion cells; only a small number of them enter the cells themselves. It is noteworthy that in the early stage, when a large number of the leukocytes have already left the thickest part, the blood vessels may still remain entirely free from infiltration. Generally, the leukocytic reaction remains at the places where the parenchyma is broken up. Only occasionally is it observed in the meninges or in the spinal ganglia. Within a few hours after the first manifestations of paralysis, the process passes more and more into a lymphocytic stage. It goes parallel with the cytolytic changes of the pleocytosis in the cerebrospinal fluid. Next to the tissue infiltration there develops a perivascular increase of cells. The meninges are nearly always infiltrated, more over the base of the brain than over the hemispheres, and more in the sulci than in the gyri. The meningeal reaction is more pronounced in the cord than in the brain.

The glial reaction appears early. That the activity of the microglia is very likely independent, that is, that it is not dependent on the breaking up of the parenchyma, is indicated first by the intensity of the reaction and then by the fact that glial proliferation is often found without any parenchymal destruction. In agreement with Spatz, Pette assumes that it depends on the direct action of the spreading virus on the tissue. The glial reaction has areas of predilection as has the destruction of the parenchyma. This is as characteristic of poliomyelitis as it is of other infectious diseases of the central nervous system, epidemic encephalitis, rabies and Borna's disease. The glial proliferation and the parenchymal destruction do not run parallel, above all not in localization. To the clinician the essence of all disease processes lies in the symptomatology, and above all this is determined by the parenchymal destruction.

The extension of the process was found not to depend on the mode of inoculation, whether cerebral, neural, nasal or gastro-intestinal. If the destruction of the parenchyma, that is, the neuronophagia, is made the basis of the discussion, the anterior horns of the cord represent the area of predilection of the process formation. In the medulla the process loses in intensity and even more in the pontile area. From here on the centers most affected are the motor nuclei and Deiters' nucleus, the intensity varying from case to case. In a few cases the cerebellum is involved, mainly the nucleus dentatus.

The glial reaction is considerably diffused. Here, too, the area of predilection is the gray substance of the cord, and the anterior and posterior horns are equally involved. In the white substance, even in severe cases, there are only occasionally some small glial lesions. In the medulla the process extends over the entire gray substance. The process is especially severe in the floor of the fourth ventricle.

In all cases there are small glial lesions in the inferior olive, but no neuronophagia. In the cerebellum the nucleus dentatus and the surrounding area form the region of predilection for the glial proliferation. The tegmentum of the pons partakes regularly in the process. On the other hand, the nuclear area of the pons is always intact.

The midbrain, if the process reaches it at all, may be severely involved, but never as much as the fourth ventricle. Darkschewitsch's nucleus and the oculomotor nuclei are more severely involved than the corpora quadrigemina, nucleus ruber and corpus luysii. The substantia nigra was in no case found to be more involved than the rest of the midbrain. It is noteworthy that in a monkey that survived the inoculation for thirty-five days the substantia nigra was infiltrated with lymphocytes and the ganglion cells were unaffected.

The infundibular region is always intact, as are the corpora mamillaria. The immediate neighborhood of the third ventricle and the tissues lying to the side of it up to the nucleus paraventricularis never partake in the disturbance, nor does the nucleus supra-opticus. In the thalamus, the central parts (the massa intermedia) are preferably involved. The ganglia habenulae were always found intact, but a few times changes were observed in the ventrolateral nucleus. The zona incerta and the nucleus of Forel's field are nearly always markedly affected. The medial and lateral geniculate bodies are spared in all cases, but the corpus pregeniculatum not so regularly. Real neuronophagia was seldom observed in the affected nuclear areas.

The neighborhood of the lateral ventricles was found intact in all cases. The nucleus caudatus never showed glial disturbance, the putamen only sparsely in a few cases. This was not so, however, with the pallidum; here scattered glial lesions were repeatedly found, but leukocytic neuronophagia here also was the exception.

The frontal part of the brain in the animals inoculated cerebrally seldom showed changes.

The anterior central convolution appears to be an area of predilection. The lesions generally are limited to the third and fifth cortical layers. Pette observed leukocytic neuronophagia of the pyramidal cells a few times, but more often he observed an accumulation of leukocytes in the immediate neighborhood, while the ganglion cells remained intact. The temporal area and the cornu ammonis were seldom involved.

The mesodermal reaction on the part of the vascular apparatus differed from case to case. Perivascular infiltration, mainly with lymphocytes, was found regularly; leukocytes were more seldom found, not only in the areas where glial proliferation took place, but also at a distance from it; the infiltration was especially abundant in the white substance of the cord.

In his summary, Pette points out that the parenchymal process and the glial reaction have areas of predilection in the central nervous system. They do not run parallel in regard to localization.

Comparison of the extent of the process in poliomyelitis and in epidemic encephalitis, rabies and Borna's disease, when this is limited to the brain stem and the medulla, shows considerable analogies, in that definite nuclei partake regularly in the development of the process. The difference is found especially in the appearance of neuronophagia, which in poliomyelitis may reach a degree not observed in the other diseases. The very high degree of neuronophagia appearing in the early stage permits the conclusion that the virus possesses a decided affinity for definite nerve cells. For the variation in the severity and extent of the process, the mode of inoculation, the virulence of the agent and the reactive power of the affected organism are responsible.

As to whether the extension of the process is primarily the result of an affinity of the virus for definite tissue areas, or whether the fluid route or an extension through the fluid (as Spatz maintained) plays a part, the observations in one case are important. In a monkey that was inoculated intravenously and was killed five days later, there was found principally the same distribution as in animals that

were inoculated by the cerebral, neural or mucous route. This is true above all of the distribution of the process in the brain stem and medulla. That in this case the distribution of the virus followed the blood and not the fluid route is indicated by the fact that, aside from the aforementioned areas of predilection, the white substance of the cord was in places affected and always perivascularly. In the same case there was considerable mesodermal and glial reaction, while leukocytic neuronophagia was completely absent. Consequently, this case indicates that for the localization of the process the affinity of the virus for the next biologic center is of the utmost importance. That the fluid, particularly the lymph route, partakes in the distribution of the virus must be admitted. But it has no more part here than in any other disease of the central nervous system caused by a living agent.

Postvaccinal Encephalitis in Holland. Dr. L. Bowman, Utrecht, the Netherlands.

During a recent smallpox epidemic in Holland, when a large number of people were vaccinated against this disease, it was found that postvaccinal encephalitis always developed after vaccination even in revaccinated persons. The cause cannot be attributed to a particular stock vaccine, since encephalitis developed after the use of various stocks of vaccine, even those which had not passed through the rabbit and stocks brought from other countries, which apparently in other countries had failed to cause encephalitis. Many experiments with animals failed to give a typical histologic picture of the disease. Hoelin found the following method: Nasal mucus from a patient with encephalitis is mixed with rabbit's serum, and to this is added dextrose; the mixture is cultivated and then, after ultrafiltration, is injected into the blood stream of a rabbit. An encephalitis develops, but does not correspond histopathologically with postvaccinal encephalitis in man. The same result can be secured with material from patients with epidemic encephalitis. The postvaccinal encephalitis epidemic in Holland has shown some changes in the histopathologic picture in the course of time. During the first years of the epidemic there was only swelling of the ganglion cells (many took on fat which apparently came from the myelin and the axis-cylinder degeneration); in later cases disturbances of the vascular walls were observed (infiltrated glia cells outside the walls), and lymphocytes and plasma cells and even polymorphonuclear leukocytes were found.

The Treatment for Tabes. Dr. A. Hauptmann, Halle.

Hauptmann reports the findings in fifty-eight patients with tabes treated within the last two and a half years. Most were given malaria therapy, followed by arsphenamine; a few patients were treated with proteins. Most of the examinations were made soon after the treatment. Of the patients treated, fifteen remained uninfluenced. The symptoms increased in two cases of optic atrophy, in five cases of convergence reaction, in one of ataxia and in one of disturbance of gait. Improvement was observed: in ataxia, eleven cases (18.9 per cent); in lancinating pain, eight instances (13.7 per cent); in gastric and other crises, seven instances (12 per cent), and in sensory disturbances, six instances (10.3 per cent). It is to be observed that the lancinating pain always increased during the course of treatment.

The patients with minor symptoms also showed some improvement: two with ptosis, one with trigeminal and one with facial disturbance, one with visual disturbance, one with a reaction to light, one with a convergence reaction, one with the achilles reflex and one with bladder disturbance.

Most noticeable were the improvements in the cerebrospinal fluid. The cell count improved in 100 per cent, the mastic curve in 77.7 per cent, the Wassermann reaction of the spinal fluid in 50 per cent and the albumin content in 44.4 per cent. The Wassermann reaction of the blood showed improvement in 11.1 per cent. The improvement in the cerebrospinal fluid was generally found to parallel the

clinical improvements. At times a clinical improvement was observed without any improvement in the cerebrospinal fluid, and vice versa.

The clinical improvement was not entirely in relation to the severity of the actual case, although in general the improvement took place in the earliest cases. No relation could be established between the improvement and former treatment for syphilis or tabes.

With the exception of one case, Hauptmann denies the possibility that his reported cases may have been cerebrospinal syphilis instead of tabes, which would account for the improvement as a result of treatment. He is likewise of the opinion that treatment in such cases is worth while.

In commenting on the improvement in the symptoms, Hauptmann is of the opinion that the lancinating pain and the crises are to be considered as due to irritation. They are the expression of inflammatory processes of the roots, or an irritation caused by substances which, as a result of the increased permeability of the blood-spinal fluid barrier, enter into the cerebrospinal fluid. When, as a result of treatment, the inflammatory products disappear and there is an improvement in the blood-spinal fluid barrier, this explains the disappearance of the disease manifestations. Therefore, this cannot be spoken of as a regeneration, but is rather a "reversion." However, it cannot be denied that the damaged posterior roots partly recover as a result of removal of the injurious influence. This may account for the improvement in the sensory disturbances. Here one must also consider reorganization. The improvement in the ataxia can be spoken of as a regeneration.

The disappearance of the symptoms is not permanent. The crises and lancinating pains return in nearly all cases. The longest time during which they remained absent was six months. None the less, Hauptmann thinks that there is no need for pessimism. In such cases one must be satisfied when one can bring the process to a standstill. That this is possible the results in the treated and untreated patients will show. Hauptmann knows of cases that have shown a normal spinal fluid for years, and although the patients may occasionally suffer from lancinating pains or from gastric crises, he considers them as cured. An occasional attack of gastric crisis or lancinating pain is not always to be considered as an expression of the persistence of the tabetic disease process. Hauptmann is more inclined to believe that it is the result of irritation of the damaged roots by foreign substances in the spinal fluid. When the increased permeability of the blood-spinal fluid barrier is not completely controlled, it permits such foreign substances to enter the spinal fluid from time to time, and must lead to irritation of the injured roots. Gastric crises and lancinating pains often follow an attack of gastro-intestinal disturbance or overindulgence in alcohol, which help to support this theory. At times the attacks are relieved by treatment with calcium, which brings about an improvement in the permeability relations. Hauptmann concludes that the treatment for tabes does not bring about a regeneration, that reorganization is to be considered and that in many cases reversion takes place.

Book Reviews

Konstitutionstypen der Kinder. Mit einem Vorwort von E. Kretschmer. By Dr. W. S. Krasusky, Odessa Price, 4.20 marks. Pp. 62. Berlin: S. Karger, 1930.

In his investigations of the problem whether Kretschmer's constitutional types, with their respective specific character traits, may also be differentiated in children, Krasusky was particularly interested in the problem of the rôle of dynamic factors in the formation of constitutional types. Age, sex, behavior, mental and physical status, living and working conditions and social factors have been investigated conjointly with the study of the psychophysical constitution. Eight hundred children were studied, including 100 under 4 years of age, 100 between 4 and 8 years, 100 between 14 and 16 years, 100 delinquents who had been committed mainly for theft and 200 abandoned, homeless children who had lived on the streets for a certain length of time. Finally, the investigation was extended to psychotic and mentally retarded children.

In this study, the following procedure was applied: general physical and anthropometric examination; observation of the children and the securing of data from those in contact with them in order to get a clear picture of their character peculiarities. In certain children, mainly in retarded and homeless ones, the natural collective experiment, using the method of Lasursky, as modified by Schewaljowa, was performed. Again, in a certain number of cases the blood groups were determined. The author emphasizes that the results obtained in this study do not refer specifically to hereditary traits; for, in his understanding, the so-called constitution of a person at a given time consists of both the hereditary endowment and the acquired character.

A special study was made of the height of the children (preschool children, school children and adolescents). In 1924, 300 children from 4 to 16 years of age were studied. The investigator noted that the growth remained below the normal standards, especially in the older children. The explanation offered for this fact is that a large part of the lives of these children had coincided with the period of the World War and the subsequent civil war in Russia, an unsettled period with scarcity of food and attendant misery. In 1926, 200 homeless children were studied. In this group, children under the age of 10 years remained further below the standard of growth than children of the same age in the previous group. This is evidently due to the fact that the living conditions of these abandoned children were much worse than those of the children of the first group. Finally, similar studies were carried out on children in a nursery, on delinquent children and on psychotic children, all of them of school age. In this heterogeneous group, the abandoned and especially the psychotic children were markedly less developed than their fellows in the nursery. Here, again, the different living conditions in these three groups of children must account for the differences in growth.

With regard to the cardinal problem of constitutional types in children, only few data are available in the literature. These data suggest that constitutional types may already be detected in very early childhood; moreover, one also may find in a great number of cases a distinct correlation between the physical type and certain character traits.

In his group of prekindergarten children (1½, 2, 3 and 3½ years old) Krasusky could not determine the constitutional type in 46 per cent of the cases. Of the remaining 54 per cent, the pyknic type was found in 34 per cent and the asthenic in 20 per cent. Certain peculiarities in the behavior of the children suggested clearly the predominance of certain traits, either of the schizothymic or of the cyclothymic character. Correlations between the bodily and the character type were noted in 65 per cent of the cases. It is noteworthy that among those cases

in which the bodily characteristics were not marked enough to present a certain type, and those in which mixed types were recognized, the cyclothymic character prevailed in a great number of cases.

The constitutional types in 100 children between 4 and 8 years of age are distributed as follows: pyknic type, 35 per cent; asthenic type, 21 per cent, and mixed types, 44 per cent. The latter may be subdivided into two groups: (*a*) pyknic type with asthenic disposition, 29 per cent; (*b*) asthenic type with pyknic disposition, 15 per cent. In 74 per cent of the cases of this group, the character was found to correspond with the constitutional bodily structure.

Two of the four constitutional types of Kretschmer—that is the dysplastic and the athletic types—have been found in a well differentiated form in only a very small percentage of the children in this group. Much oftener, certain dysplastic and athletic features have been observed to be more or less conspicuous in children with a dominant asthenic or pyknic foundation.

In the school children, the constitutional types presented themselves as follows: asthenic, 20 per cent; pyknic, 29 per cent; asthenics with pyknic deviation, 23 per cent, and pyknics with asthenic deviation, 20 per cent. A correlation between the bodily structure and the character type has been observed in 79 per cent. The adolescent group comprises the following constitutional types: asthenic, 40 per cent; pyknic, 38 per cent; asthenic with pyknic disposition, 10 per cent, and pyknic with asthenic disposition, 12 per cent. A correlation between the bodily type and the character type was noted in 75 per cent of the cases of the group.

A comparative study of the constitutional types in the aforementioned four groups of children of different ages brings forth the following interesting facts: Whereas the percentages of various bodily types are markedly different in these groups, the correlations between the bodily and the character type are presented by percentages fairly close to each other. This parallelism between the character and the bodily features, which appears to follow its constant course as the child advances in age, accounts for the almost constant relationship mentioned between the body and the character type in the children of different ages. This parallelism, in Krasusky's belief, is the result of the coordinating function of the endocrine glands. The latter would represent the central regulator, assuring continuity of the psychophysical unity of the organism.

When one considers the distribution of the constitutional types in 300 children ranging between the ages of 4 and 16, one notices the following characteristic features: The number of pyknics diminishes and that of asthenics increases as the children advance in age. The mixed types also follow the age, reaching the comparatively lowest percentage at the age between 13 and 16. Here again, Krasusky stresses the rôle of the endocrine system as a regulator of growth and development. He holds this system and the biochemical processes of the organism responsible for the already mentioned shifts in the frequency of constitutional types in relation to age. In favor of this view are, according to Krasusky, experimental studies and clinical observations demonstrating the part that the thyroid, hypophysis and other endocrine glands take in the growth and general development of the organism.

The investigations carried out on 200 homeless and 100 delinquent children gave the following results: (*a*) Delinquent group (100 children): asthenic, 52 per cent; pyknic, 24 per cent, and mixed types, 24 per cent. The character types are presented by schizothymics, 68 per cent; cyclothymics, 16 per cent, and mixed types, 16 per cent. (*b*) Homeless group (200 children): asthenic, 55 per cent; pyknic, 25 per cent; mixed types, 20 per cent; schizothymic character, 72 per cent; cyclothymic, 15 per cent, and mixed types, 13 per cent.

One notices that in these two groups the distribution of the bodily and the character types is nearly the same. A correspondence between the bodily and character traits was found to be less frequent in these children than in those of the other groups, 61 per cent in the homeless and 58 per cent in the delinquent children. Another marked phenomenon in this category of children was the comparative frequency of dysplastic features, usually grafted on an asthenic background. The asthenic type with the associated schizothymic character was found to be far more frequent in these two groups than in the foregoing groups. It is the author's

contention that this is due both to the influence of the extremely unfavorable milieu, these children come from, and to their life on the street. The living conditions of these children do much to favor the development of schizothymic characters.

The rôle that paratypic factors (social factors, physiologic and biochemical processes and diseases) appear to play in the development of constitutional types is illustrated by the two following cases of a boy, 9 years of age, and a girl, 7 years of age, when first seen in 1924:

1. The boy was a typical pyknic-cyclothymic. Four years later, he had lost many of his pyknic and cyclothymic features and acquired many peculiarities of the asthenic-schizothymic type, so that now (in 1928) he is a typical representative of the mixed constitutional types.

2. The girl, from a very marked asthenic-schizothymic type, turned, within the same four years, into a mixed type with dominant pyknic-cyclothymic features.

The last two groups of children investigated by Krasusky consist of: (*a*) 35 psychotic children and (*b*) 65 mentally retarded children. Among the psychotic children bearing the diagnoses of "dementia praecocissima," epilepsy, psychopathy, early circular psychosis, etc., there were: asthenic, 69 per cent; pyknic, 10 per cent, and mixed types, 21 per cent. The distribution of the constitutional types in the group of mentally retarded was: asthenic, 50.7 per cent; pyknic, 18.6 per cent, and mixed types, 30.7 per cent. These two groups of children have one common character, which is the high percentage of children with dysplastic features, 56 per cent among the psychotic children and 52.3 per cent among the mentally retarded. Among idiots and imbeciles, the percentage was still higher—70 per cent.

There were other distinctive characters worth noting: In contrast to the observation that among normal girls the asthenic types are more numerous than among normal boys, among the mentally retarded girls the pyknic types with the corresponding cyclothymic characters are more numerous than among the retarded boys. The athletic type was observed in a few cases only, and oftener among boys than girls.

With regard to the study of the character types, one should realize that such a study was greatly handicapped by the mental condition of the children. It was nevertheless clear that schizothymic types dominated the psychotic group, being represented there by 60 per cent, whereas the cyclothymic and mixed types were represented, respectively, by 14 per cent. In the group of mentally retarded children, schizothymic features were noted in 46 per cent, cyclothymic in 31 per cent and traits of the mixed type in 22 per cent. In these two groups of children the asthenic type with the corresponding schizothymic character is the dominant type. It must be added that certain character peculiarities of the retarded children make them quite different from the representatives of the same types among normal children. Thus, the positive features of cyclothymia when overdeveloped take an antisocial character; the features of the schizothymic type turn into more or less pronounced negativism accompanied with high irritability. In girls there also develops a tendency to hysteria in a great number of cases. A relation between the bodily type and certain definite peculiarities of character was observed in 56 per cent of the psychotic and in 62.9 per cent of the mentally retarded children.

Krasusky was also interested in the study of the blood groups in the normal and abnormal children. So far, four groups have been singled out in human beings. The distribution of individuals of a certain region—with regard to blood groups—appears to remain constant. The determination of the blood groups in psychotic children presents a particular interest in the light of certain studies of blood groups in psychotic adults. It has been found that in mental diseases, and particularly in schizophrenia, there is an increase of representatives of group I and a decrease of those of group IV, as compared with normal persons.

A similar distribution of the blood groups was observed in the psychotic children, as compared with the distribution of blood groups among normal children of the same region. (The normal standards were established by Dr. D. A. Barstein.) The mentally retarded children showed a distribution of blood groups

similar to that observed in the psychotic children. Here the deviation from the normal standards was still more pronounced.

In contrast to these findings are those obtained among the delinquent children: the blood group distribution proved to be essentially the same as in normal persons of the region in which these investigations were carried out. These findings as well as the data available in the literature demonstrate, in the author's belief, the following phenomenon: The constitutional chemical process, as a genotypic factor, corresponds to those modifications of the psychophysical constitution which have a background in the hereditary genotypic character. In those cases in which the deviations from the normal were assumed to be of the paratypic character, no abnormality in the constitutional chemical processes could be detected.

In concluding, Krasusky expresses his conviction, derived from this study, that the constitutional factors should be considered in the pedagogic activity more extensively than they have been heretofore. The forming of the personality of the child should be the common work of the physician and the pedagog.

The Technique of Psycho-Analysis. By Edward Glover. Price, 6 shillings. Pp. 141. London: Baillière, Tindall & Cox, 1928.

That only serious and attentive students may derive benefit from this book, the author (Ernest Jones announces in the preface) has avoided simplicity of presentation. Although intended for the advanced scholar, the text, by virtue of precision in word choice and concreteness of illustration, may be enjoyed by the elementary student of psychoanalysis as well. In his first chapter, the author calls attention to certain practical points: He suggests that the business details of the analysis be introduced early in the course of treatment, and hints that it would be well for the patient to be allowed to think that the analyst is a very busy man. To the patient's inevitable inquiry as to the duration of the study, the therapeutist is urged to give equivocal answer; this is justified by comparison with similar prognostic responses given by the ordinary medical clinician who surely does not promise to relieve his patient of heart disease or gastric ulcer in any specified time. An entire page is devoted to the momentous question of whether the analyst should greet the patient with a hand-shake. Certain common difficulties are reviewed, such as the problem of the patient who makes associations too readily, the management of the subject who calls for help when his association formations stumble, and the handling of the persistently taciturn patient. The analyst, Glover warns, should avoid technical terms, as these are often taken by the patient as new toys with which he can play. The therapeutist must be on the watch for resistance, an obstacle that may be evidenced equally well by repeated tardiness or unswerving punctuality. In his discussion of sublimation, the author takes in a large territory, suggesting that "all cultural activities of mankind, both creative and imitative, constitute true sublimation." On one occasion at least, Glover becomes impatient with his Master, thinking that Freud's characterization of anxiety is a feeling of psychic helplessness in the face of overwhelming disaster is too simple.

The examiner who finds himself repeating stereotyped activities or who feels that he must rationalize his own difficulties or silence during a treatment is probably subjecting the whole process to subjective distortion. The best prophylaxis against this unconscious bias is previous perfect analysis of the analyst himself, so that, in Glover's term, he may be "pure by virtue of castration." The transference neurosis is the subject of a chapter. Owing to the fact that early in the course of treatment many transferences occur which resemble the transference neurosis, the latter may not be recognized when it is reached. Yet unless the patient has awareness of this phase—not only consciousness, but conviction as well—the psychoanalyst will fail. The author postulates that all analytic manifestations occurring during this stage relate to the transference neurosis. When the therapy is being terminated, the transference must be dissolved. The family medical practitioner, Glover charges, unconsciously but definitely maintains the patient's transference to himself after the acute stage of the physical illness is over. The psychoanalyst, however, must be bolder. Good intentions are not

enough; the examiner must know that the transference should be dissolved, not when the superficial symptoms have been dissipated, but only after exhaustive libido analysis and ego analysis have been completed. That this stage has been reached is indicated by such phenomena as a cessation of the patient's demands on analytic protection, by a "levelling down" of dreams, by a clarification of many screen memories and by an advancing social adjustment. The technic of dissolving transference is not described, a disappointing omission in view of the practicalness of the book as a whole.

The development of "active therapy" through Freud and Ferenczi is traced, and the advantages and dangers of this variation are discussed. Glover, although not entirely discarding it, warns against its excessive, uncritical or incautious use. The final chapter, entitled "Analytical Crises and Exceptional Cases," contains a miscellany of practical hints about the management of certain unusual situations. The author describes the management of nonneurotic patients with bad emotional adjustment; with melancholia as an example, he discusses the psychoanalysis of patients with mental disease.

In spite of the abstruseness of his topic, Glover writes in an easy style, displaying happy word choice and lucid phraseology. His fluency sometimes approaches glibness. The book is so practical that it must constitute a valuable manual in the library of the practitioner of psychoanalysis. In common with other freudians, Glover has made a contribution to physical medicine by stressing the personal and psychic sides of the patient's problem; his epigram that, after an ordinary clinical interview, the patient "bitterly resents the assumption that his relation to his disease is simply that of a carrier" should be before the physician in all his contacts with patients.

Speech Pathology. By Lee Edward Travis, Ph.D. Price, $4.00. Pp. 331. New York: D. Appleton & Company, 1931.

This interesting book on speech pathology deserves attention because its presentation is different from that usually found in the treatment of this subject. The author discusses the whole realm of speech pathology. He begins with the neuromuscular basis of speech. In this he reviews the usually accepted theories and states that in the present work he emphasizes "the theory that in every activity every part of the central nervous system functions under a dominant gradient. Subcortical as well as cortical mechanisms participate in every act of the organism." He then elaborates Orton's theory of cerebral dominance.

In the next chapter on the classification of speech disorders, he states that this problem may be approached in different ways: the neurologic, the pathologic, the clinical and the psychologic. He wisely emphasizes, however, that any attempt at grouping speech disorders under sharply distinct heads must be only tentative and imperfect. Nevertheless, for the aid of students he publishes in full the classification of speech disorders published in S. M. Stinchfield and S. D. Robbins' "Dictionary of Terms Dealing with Disorders of Speech." It is a question whether this classification will do anything but confuse.

In a discussion of the general causes of speech disorders, he mentions the influence of organic factors. The unusual part of this chapter is in the discussion of the importance of the intra-uterine state, and the possible effects of fetal positions on speech development. There is an interesting discussion on handedness and its relation to speech. This subject has by no means been settled, and it is possible that further studies may modify existing ideas of the determining factors in right and left handedness.

The methods of general examination are well presented. The author's theory of stuttering is that in most cases it is a neuromuscular derangement secondary to a general reduction in cortical lead control. The latter is conceived to be due to transient and mutual inhibitive activities of the right and left cerebral hemispheres. In other words, the symptoms of stuttering are "mainly the peripheral signs of rivalry between the two sides of the brain."

The author discusses such other organic causes as injuries to the brain, and so on, which may bring about stuttering. He gives three case histories of stutter-

ing, in each of which there was a shift of handedness, in which a correction of handedness caused a disappearance of the stuttering.

The chapter on disorders of articulation and phonation is well presented. The next chapter on aphasia and kindred disorders is merely an abstract of Head's point of view, and presents no opinion of the author. The last chapter is a summary. The appendix contains stimulus syllables, words and sentences for speech training.

The whole basis of the author's thesis is dependent on the acceptance of the theory of cerebral dominance. If this theory can be upheld by practical experience with stutterers, then it will constitute a distinct contribution to knowledge of the physiology of brain function. Success has not always been obtained by such methods. Moreover, the theory of cerebral dominance does not rest on firm ground. However that may be, this is a stimulating book.

One would wish that a glossary in a neurologic textbook were unnecessary. In the present book it is obviously needed, for the average physician or student could hardly be expected to know the meaning of the words "agitographia," "agitophasia" and so on. Some of the neurologic definitions are not quite accurate; for example, the definition of Friedreich's ataxia. Paralysis is defined as "a loss of motion or sensation in a living part or member of the body."

L'hérédo-syphilis mentale. By P. L. Drouet and J. Hamel. Price, 30 francs. Pp. 205. Paris: Masson & Cie, 1930.

In this 205 page monograph, Drouet and Hamel discuss the general question of heredosyphilis, emphasizing especially its biologic, diagnostic and psychopathologic aspects. Their work has been very well done and amply repays careful reading. The ground is covered most thoroughly, including full consideration of the contributions and conclusions of others as well as personal findings. Furthermore, the presentation is gratifyingly direct and clear, and the arrangement of the material is extremely good, with an excellent appended bibliography.

The subject matter is organized under the following chapter heads, all of which are fully and illuminatingly developed: the rôle of heredosyphilis in psychopathology, diagnosis in childhood and adolescence, diagnosis in adulthood, relation (general) to mental disorders, psychiatric (systematic) aspects of heredosyphilis, social considerations, prophylaxis and treatment.

The section on diagnosis appears of particular interest and merits special comment. Among children and adolescents, the authors find of great significance certain stigmas, chiefly cranial, dental, facial and teratologic (mainly absence of xyphoid), with a significant percentage (16), however, in which stigmas are absent. As to serology in this group, the Wassermann reaction of the blood seems important and is positive, usually mildly, in most instances. The Wassermann reaction of the spinal fluid is frequently positive likewise. Important, in addition, in the fluid are increased pressure, pleocytosis and increased solids, with in general, as far as the authors' series is concerned, the serology positive in at least one particular in 91.6 per cent of the cases. Respecting clinical signs among adults, cicatrices of old lesions in various fields are of some significance, but more so cranial, dental, cutaneous and facial stigmas. Of importance in adults, too, are fistular adenopathy and certain neurologic phenomena as hemiplegia, paraplegia, syndromes of the type of Little's disease and convulsive reactions. As regards serology, essentially the same findings obtain as for children and adolescents. Also, endocrine changes dependent on the underlying syphilitic process are exhaustively analyzed and their importance as part of the total picture, in both age groups, strongly stressed.

Interesting further is the authors' relation of heredosyphilis to the category of degenerative agents in a broad sense, correlating on that basis the commonly noted stigmas and dystrophic effects somatically, with various forms of imbalance and disequilibrium psychically, and predispositions to actual and frank process psychoses of both major and minor types.

Die Neuropathischen Knochen- und Gelenk-Affektionen. Deutsche Orthopädie. Volume 8. By August Blencke and Bernhard Blencke. Price, 44 marks. Pp. 304. Stuttgart: Ferdinand Enke, 1931.

This book gives an excellent summary of the knowledge of the neuropathology of bone and joint diseases. The work is divided into four parts. There is first a general introduction under which is discussed the clinical occurrence of such diseases, followed by the pathology and therapy.

The second and main portion of the book discusses these diseases in the skull, vertebrae and sternum, upper limbs, pelvis, hips, thighs, knees, legs and feet. The relation of these diseases to trauma follows. The last part gives the literature. There are twenty-four pages of references. This, in itself, is evidence of the wide interest this subject has always aroused, and is also an indication of the literature consulted in the preparation of the book.

In the first part no general classification is adopted, but that of Israel is favored. Israel divided orthopedic disturbances as occurring in: (1) brain disease and (2) spinal cord disease. In the first type are mentioned dementia paralytica and hemiplegia, and in the last, congenital deformities, such as meningocele, tabes, syringomyelia, transverse myelitis and spinal cord injuries, and lastly, those occurring in peripheral nerve conditions.

In a discussion of the pathology, a distinction is made between arthropathies occurring, for example, in tabes and syringomyelia, and those joint conditions that are really part of an arthritic process. It can at once be said that there is no definite knowledge as to the exact pathologic cause of arthropathies. In a discussion of the joint conditions occurring in various parts of the body, nothing is found wanting. The therapy, particularly from the orthopedic standpoint, is well presented, as is the discussion of the relation of trauma to these conditions.

The book is abundantly illustrated, there being altogether 214 illustrations. If there is any criticism of the work, it lies in the fact that the illustrations have no captions, they being referred to in the text, and second, that there is not sufficient outline of the details of the work, either in the beginning or in the end of the book, so that the actual subject under discussion is to be found under each individual page. A better index would make the book infinitely more valuable.

Nervous Indigestion. By Walter C. Alvarez, M.D. Price, $3.75. Pp. 297. New York: Paul B. Hoeber, Inc., 1931.

This is a very interesting and stimulating work. The author obviously has a wide understanding of the psychology of his patients and knows how to handle them. To him not every symptom necessarily means an organic disease, nor does every organic symptom necessarily mean a functional condition. The reviewer, who has practiced neuropsychiatry for many years, is in full agreement with the author's point of view, with the exception, however, of the last paragraph in the preface when he states that he agrees with Cabot that "much of the work might perhaps be done by trained social workers." This is vicious advice, for while very rarely a social worker may turn out to be everything a physician desires, most of them, with insufficient training, assume that they know more than the physician. In fact, the whole plea of the author's book is for the education of the physician and the medical student in the psychoneuroses. Why, therefore, destroy it by the use of social workers?

The Creed of a Biologist. By Alfred Scott Warthin, M.D., LL.D. Price, $1.50. Pp. 60. New York: Paul B. Hoeber, Inc., 1930.

Elderly philosophers tend to write essays on the meaning of the universe. Other elderly philosophers read them and agree or disagree with the opinions given, but the young, knowing more than the old, do not pay much attention. Dr. Warthin flatters man. He says "Man must have some kind of an answer to the eternal question of Whither, When, and Why." This may be true of man, but it is not true of most men, who are really children; they accept what they were taught and think and wonder not at all.

But all scholars, and of course all physicians are scholars, will read Dr. Warthin's essay and his creed, on the last page, with pleasure. Few will subscribe to it in its entirety. A few will even say that the jargon of science is not any truer than the jargon of theology. The essay is not only worth reading, but worth owning.

The Nervous System. An Elementary Handbook of the Anatomy and Physiology of the Nervous System for the Use of Students of Psychology and Neurology. By James Dunlop Lickley, M.D. Second edition. Price, $3.50. Pp. 137. New York: Longmans, Green & Company, 1931.

The first edition of this book appeared in 1912; therefore, the second edition is really in a sense a new book. In the 137 pages the author has presented in a very simple and direct manner the chief anatomic and physiologic functions of the central nervous system. There are 117 illustrations, many of which are in colors. Besides, there are many explanatory tables of the course of the fibers, such as the sensory and motor, cerebellar and so on. The reviewer knows of no small book in which the illustrations and tables have been so well conceived and selected. The text is also adequate for the purpose. The book can be recommended to students of psychology and neurology.

News and Comment

THOMAS W. SALMON MEMORIAL LECTURES

The first series of The Thomas W. Salmon Memorial Lectures will be given at the New York Academy of Medicine, 2 East 103rd Street, New York, on April 8, 15 and 22, at 8:30 p. m., by Dr. Adolf Meyer, professor of psychiatry, Johns Hopkins University, and director of the Henry Phipps Psychiatric Clinic, Baltimore. The subject will be "Psychobiology." In the first lecture he will discuss the relations between psychiatry and general medicine and associated sciences, and the meaning of the "personality function" to the psychiatrist. The second lecture will present a concrete picture of some specific problems, such as the schizophrenic reactions, with a statement of the essentials of Dr. Meyer's deductions from his studies for a fundamental understanding of psychiatric diseases in general. The third lecture will deal with psychiatric therapy; the relationships with psychoanalytic and other therapeutic approaches will be defined and a picture formulated as to present-day thought and practice in psychiatry.